# POTENTIAL HEALTH HAZARDS OF COSMETIC PRODUCTS

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# HEARINGS

BEFORE THE

## SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

OF THE

## COMMITTEE ON SMALL BUSINESS
## HOUSE OF REPRESENTATIVES

ONE HUNDREDTH CONGRESS

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# POTENTIAL HEALTH HAZARDS OF COSMETIC PRODUCTS

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## THURSDAY, JULY 14, 1988

House of Representatives,
Subcommittee on Regulation
and Business Opportunities,
Committee on Small Business,
*Washington, DC.*

The subcommittee met, pursuant to notice, at 10:54 a.m., in room 2359, Rayburn House Office Building, Hon. Ron Wyden (chairman of the subcommittee) presiding.

Members present: Chairman Wyden and Representative Flake.

Chairman Wyden. The Subcommittee on Regulation and Business Opportunities will come to order.

Today the subcommittee begins a series of hearings to examine health and safety questions posed by the $17 billion U.S. cosmetics industry.

Millions and millions of Americans, of course, are exposed to these products every day, and a growing body of evidence suggests that some of these common products, and their ingredients, pose serious health hazards.

Yet few if any of the chemicals have ever been banned as cosmetic ingredients. Thousands of small businesses across this country—beauty salons, barber shops, small retail stores, and beauty schools are now selling and using countless cosmetic products.

Just like millions of cosmetic users and workers in this field, these small businesses are relying on the Government to ensure their safety and effectiveness.

Contrary to what is popular belief, the Federal Food and Drug Administration does not test cosmetics for safety as it does food and drugs.

The FDA does not have the authority to require that manufacturers prove the safety of products before their marketing.

Incredibly, there are only two actions the Federal Food and Drug Administration can take to protect the consumer. Occasionally, they take a contaminated batch of products, and ask manufacturers to change their advertising claims.

Even if the agency suspects that serious adverse health effects are caused by a cosmetic product, the agency can't ask for ingredient information from the manufacturer to determine the formulation, or require that the manufacturer provide test data to prove the product safety or efficacy.

In short, the burden of proof lies on the Government's shoulders, despite the fact that vital information about these potentially dangerous products is being withheld from regulators.

In my view, these regulatory gaps raise serious questions about the Food and Drug Administration's ability to effectively oversee the cosmetics industry in this country.

The Food and Drug Administration has told the subcommittee staff that nearly 4,000 different chemicals are used in cosmetics, and another 4,000 are used in fragrances.

These are mixed to form up the 40,000 combinations used in a wide variety of products. Cosmetics manufacturers aggressively market the products, and they contain chemicals that might cause cancer, birth defects, central nervous system disorders, skin and eye irritations, allergic reactions, and other acute toxic effects.

Now the Consumer Product Safety Commission has provided new information to the subcommittee, and we've analyzed it. It shows that hospital emergency rooms reported treating 47,000 cosmetic related injuries during 1987 alone.

Over 151,000 injuries occurred between 1985 and 1987, and they resulted in 2,300 hospitalizations. It was particularly of concern to the subcommittee that these injuries were caused by a whole range of cosmetic products—soaps, nail preparations, hair perms, hair straighteners, shampoos and dyes, creams, lotions, and facial masks.

Recently, many manufacturers have expanded into a new field—fountain of youth products which claim to speed up the cell renewal process, repair skin, and make wrinkles fade, or in their words, lift upward.

Notwithstanding the adage about beauty being only skin deep, the efficacy of such miraculous products would require active ingredients that would have to work well below the skin surface.

Speeding up the cell renewal process implies a procedure containing far more than a little pigment and some moisturizer.

Federal law requires products affecting the structure or functions of the human body to be regulated as drugs, and then undergo strict premarket approval to assure their safety and efficacy.

But today, the FDA has not tested one of these products to safeguard consumers. It has only instructed companies to scale back their claims about products, and has operated under the assumption that these products cause no real harm.

Unfortunately, it is our view that no one—neither the Government, nor anyone else knows what risks or adverse health effects the long-term exposure to these cosmetic ingredients may actually cost.

Today, we are going to hear from witnesses who have discovered just how dangerous these products may be. A citizen from my State will tell us about how her work with beauty parlor chemicals resulted in a chronic asthma condition.

An attorney will describe how a hair straightener ignited his client's tresses. A physician and his patient will discuss neurologic damage attributed to the hairspray used on wigs.

In addition, the subcommittee is going to hear today from Dr. Gary Grove, who will present his research on antiaging creams.

Dr. Grove will question whether these so-called cosmetics are not in fact drugs, with all the potential side-effects that can accompany drug use.

Dr. Grove is also going to testify about the similarities between many of these over-the-counter products and Retin-A, a drug that the FDA has warned physicians to use with care, and Accutane, a drug that has been linked to birth defects.

Finally, we are going to hear from Beth Shulman of the United Food and Commercial Workers Union, who is going to discuss the occupational health and safety concerns that she hears from her workers in her organization around the country.

Not only do beauticians and industry workers face potential ill-effects, they have little or no access to information about which products are the most hazardous, and how to minimize contact with them.

As the baby-boomers age, we can expect the cosmetics industry—particularly those that market fountain of youth products—to expand tremendously.

The trend certainly is very clear. In the past decade, beauty product sales have increased 100 percent. I think it is of great importance that we understand the health and safety consequences of the regulatory vacuum in which this huge and growing industry exists.

That is the point of our subcommittee's inquiry. As I have stated, this will be the first of several hearings to examine health and safety questions in this area.

I think it is very fitting that we begin today by hearing from some of those whose lives have been irrevocably changed by their contact with everyday products, and many of us, possibly mistakenly, have assumed are harmless.

[Mr. Wyden's statement may be found in the appendix.]

Chairman **Wyden**. So we welcome all our witnesses. Let me say that it is the practice of the Subcommittee on Regulation and Business Opportunities to swear all of our witnesses before the subcommittee.

Do any of you have any objection to testifying under oath?

A **Voice**. No, Mr. Chairman.

[Witnesses sworn, en banc.]

Chairman **Wyden**. Let me thank all of you for your help and assistance.

We have Beth Shulman today, vice president of professional hair care and beauty trades of United Food and Commercial Workers Union; Edith Khatami, a cosmetologist in San Francisco, CA; and Ms. Kristi Smith, a cosmetologist from my home town. I want to welcome you in particular, Kristi.

Ms. **Smith**. Thank you.

Chairman **Wyden**. Thank you for coming, and for your courage as well.

Why don't we begin with you, Ms. Shulman? We have appreciated the cooperation your organization has furnished to us.

We will make a copy of your prepared remarks a part of the hearing record in their entirety, and perhaps in the interest of time, if you could summarize your principal concerns, that would be very helpful to us.

## TESTIMONY OF BETH SHULMAN, INTERNATIONAL VICE PRESIDENT, UNITED FOOD AND COMMERCIAL WORKERS INTERNATIONAL UNION; ACCOMPANIED BY DEBBIE BERKOWITZ, DIRECTOR OF SAFETY, FOOD AND ALLIED SERVICES TRADES

Ms. SHULMAN. Thank you, Mr. Chairman.

Mr. Chairman, my name is Beth Shulman and I am vice president and director of the professional hair care and beauty trades division of the United Food and Commercial Workers' International Union.

Our union represents over 1.3 million members throughout the United States and Canada, in over 600 local unions. And as part of that international union, we represent over 40,000 hair care professionals.

The task before this subcommittee, to determine if the American public is being protected from hazardous chemicals found in cosmetics, is an urgent one.

I want to thank you for the opportunity to testify before your subcommittee on the serious health consequences that are resulting from the lack of Government regulation in terms of making sure that cosmetics are safe and effective, before they come on the market.

As director of the professional hair care and beauty trades division, I have had the opportunity to criss-cross this country.

I have gone into hair salons and beauty schools, and talked to cosmetologists and barbers throughout this country concerning what kinds of health effects they're having as a result of the products they use on a daily basis.

I can tell you, these people are concerned. There are now thousands of cosmetic products on the market today used by these workers, and used by millions of men and women in the United States.

While these products may smell nice, and are packaged beautifully, the problem is they are not benign. They are causing problems like asthma, as a witness will testify to today.

They are causing problems in terms of neurological damage, as Edith Khatami will tell you about.

They have caused skin diseases. Moreover, we are finding a problem that needs to be looked at more closely in terms of the long-term effects, in terms of reproductive hazards, and in terms of cancer.

Our files are replete with letters from members talking about these problems. A cosmetologist in Reese, MI, who has upper respiratory problems and skin diseases.

A hair dresser in Fair Lawn, NJ, had to leave the profession at age 29 because she had an asthma condition. We have a problem in Kentucky. Four out of five of the cosmetologists in a salon have had miscarriages—several of them multiple miscarriages.

In Los Angeles, we have a problem in terms of sculptured nail applications. While there is a ban on ethyl methacrylate in sculptured nails, it is being used universally in Los Angeles. The problem is that it is a neurotoxin that is causing severe health damage to the people using it.

Our position is not that chemical cosmetics should be banned. But our position is that workers and consumers alike should not be human guinea pigs when it comes to cosmetics.

Most consumers, as well as professionals, would be shocked to learn that cosmetics are not required to be tested before they come on the market.

Moreover, cosmetics are not even required to be submitted by manufacturers to the FDA for their ingredient lists or the test data that's made on them.

There is no requirement that when the manufacturers get consumer complaints that those be submitted to the FDA.

What we have is a situation of total lack of regulation. To add insult to injury, people working in the hair salons, the members that the UFCW represents, are really in a worse situation because cosmetics are not required to be labelled in the salons.

What I have before me are two hair sprays by the same manufacturer. One is required to be labelled. It is the one sold in a drug store or supermarket where all of us live. It has ingredient labelling on it.

The other one is used in the salons. This one has no labels. So a worker working in the salon has no way of knowing what's in the product they are using. They cannot protect themselves, and they cannot protect the consumers they are working on on a daily basis.

Thus, the great irony is the average consumer in some ways is at greater risk in a salon than at home.

When one looks at this, considering all the health problems that these cosmetics have caused, and the lack of regulation of cosmetics, one asks the question why—why hasn't there been cosmetic regulation?

When we look back, the last change in cosmetic regulation was 50 years ago. Scientific evidence has changed since that time. We know that cosmetics are absorbed through the skin, and go into our bloodstream.

We know that we can inhale cosmetics, and it gets into the lungs and causes asthma problems. We know it gets into our bodies and causes neurological damage today.

Moreover, what we have now is manmade chemicals, chemicals that we did not know anything about 50 years ago.

We are starting to understand that these chemicals cause health problems, and they need to be addressed.

The bottom line is that cosmetic products are chemicals. They are a mixture of chemicals. The tools of the hair care profession are chemicals—chemicals like formaldehyde, methylene chloride, ethyl methacrylate—all of these that are causing problems in terms of neurological damage, asthma, long-term effects that we do not even know today.

Despite our changing understanding that these cosmetics do cause health problems, there has been no change in the legislation for over 50 years.

We still have the same legislation that does not regulate this industry, and does not regulate the safety of these products.

The result is that workers and consumers alike are unprotected when it comes to cosmetics.

What little authority the FDA has with regard to these cosmetics they have done nothing about. Take methylene chloride. The FDA itself proposed banning this ingredient 2½ years ago. They proposed it. What's happened? It has never been banned. Methylene chloride is a suspected cancer causing agent—found by FDA to be a suspected cancer-causing agent.

What I have here is a hairspray that was bought yesterday in a drugstore in Washington, DC. What ingredient does it have in it? Methylene chloride, that same ingredient that the FDA proposed banning 2½ years ago, a suspected cancer-causing agent, according to them. It is still on the market, and has not been banned as of today.

The UFCW is a worker organization. Our task has been to make sure that the members we represent, and workers as well, throughout the United States, are protected in terms of their health and safety.

That is why we are here today. This is an industry in which the workers that work in it are not protected, and the consumers that use these products are not protected as well.

What we want to see is protection. We do not want to be human guinea pigs to the cosmetic industry. What we want to see is that people in this industry are safe in terms of their health.

What we would like to see is labelling in the salons so that workers can know what they are using and protect themselves and the public.

What we would like to see is that products, before they come on the market, be tested as to their contents, their effectiveness, and more important, their safety.

What we would like is that ingredient lists be submitted to the FDA by manufacturers and that consumer complaints be required to be submitted to the FDA as well.

What we also would like to see are studies done determining the long-term impact in terms of these chemicals, in terms of cancer, reproductive hazards, and any other illness that will not be seen for over 20 to 30 years.

What we have here is an industry that is unregulated. We have worked hard, the UFCW, to gain protections for all people.

We urge this subcommittee not to let the problems you will see today from witnesses like Kristi Smith and Edith Khatami, from doctors who will testify as to the causal relationship between cosmetics and these illnesses, die today.

We want to see change. We want to make sure that the workers and consumers alike are protected. Thank you very much, Mr. Chairman.

[Ms. Shulman's statement may be found in the appendix.]

Chairman WYDEN. Well, Ms. Shulman, thank you very much. You have given a remarkable indictment, in my view, of the current regulatory system, and some of its shortcomings. I will have some questions for you in just a moment, and I want to thank you for your help.

Let us move now to Ms. Smith, if that would be agreeable to you. We want to welcome you. You are a long way from home. I always like to have Northwest residents testify before the subcommittee.

We do have, Ms. Smith, just absolutely infernal mikes in this room. If you could pull those microphones—both of them, close to you so that we could hear better, that would be great.

Thank you very much. We will make a copy of your prepared remarks a part of the record in their entirety, and if you could summarize your principal concerns it would be very helpful.

## TESTIMONY OF KRISTI SMITH, COSMETOLOGIST, PORTLAND, OR

Ms. **Smith**. My name is Kristi Smith and I am 24 years old. I enrolled in a beauty college in Portland, and not long after I started I started feeling—I had some trouble breathing.

But at the time I really did not realize what was happening to me. As time went on, my breathing got worse and worse, and by the time I went to see the doctor, I had already gotten to the point where I had chronic asthma.

Eight months after I started I went into an emergency room because I could not breathe at all, and things kept getting worse.

Chairman **Wyden**. Kristi, excuse me. Let me interrupt you just for a moment.

You went to a hospital emergency room after you had been working with these products, or you went to the emergency room shortly after you had been working with these products?

Ms. **Smith**. Yes; after I had been in the beauty college, and been exposed to the chemicals, I went to the emergency room because I was having such a hard time breathing.

The episodes of feeling like I couldn't breath continued. It feels a lot like I am underwater when I am having my attacks.

The management of the school frowned on me leaving because I was having problems, and they would just tell me to stop complaining. They did not seem real concerned with what I was trying to express to them.

In June, 10 months later, after I had started the school, I went to another doctor, and that is when I was diagnosed that I had occupational asthma.

He told me that it was from the exposure to the chemicals at the school. They told me to take a leave of absence from the school, and eventually I chose to quit completely.

In January 1987 I went to another specialist who told me that I had irreversible asthma. It has been almost 3 years since I have had my asthma, and I am living with this condition. It makes it very hard for me to lead a normal life.

It is very uncomfortable. When I have these attacks they last sometimes for as long as a month. The last one that I had was about a month long, and I have to take medication daily.

I have to take stronger drugs at the time that I am having the attacks, and it is very hard on me because I have to try sometimes as many as 10 times to get my breath. When I try to do that it puts a strain on my muscles around my heart and in my stomach, and it just makes it very uncomfortable.

It is very upsetting. When I do not have the attacks, the appreciation of breathing is incredible. I mean, I cannot even tell you how much you appreciate breathing until you cannot breathe.

Sometimes when I go out into public, I have to be careful because you can go into public restrooms, or just past somebody who is spraying hair spray. I have to be aware at all times of my surroundings because I am petrified that I am going to come across something and another attack is going to start.

When I was—now I am 24. Not being able to finish school has ruined my career, and I feel like this has pretty much ruined my life. I am going to have to live with it forever.

There was absolutely no ventilation in the school that I was in at all, and we worked on people in the school. The only ventilation was the front door. Nobody told us at all that there was any kind of—they did not warn us at all that there could be problems. There was no labels on anything.

There was no—absolutely nothing. We got clear bottles. We had really no idea what we were using, or the effects that it could have on us in the future.

When I left the school, they tried to—I left 2 months before I was supposed to graduate. They got in touch with me. They tried to sue me for leaving the school early. I was paid up until that time.

Chairman WYDEN. Make sure I understood that. You got sick, but they tried to sue you?

Ms. SMITH. Yes; they knew why I left. They were aware that I left because I was ill. They got in touch with me about 6 months later and told me that I had a bill from the two months that I was not even there. I was paid up until the time I was there, until I left.

They wanted me to pay for those two months that I was not there. I went to an attorney with it, and we countersued them.

Chairman WYDEN. I do not want to interrupt you again, but who won the countersuit?

Ms. SMITH. I did.

Chairman WYDEN. Were there any agreements as part of the countersuit with respect to any conditions or anything in that nature?

Ms. SMITH. I am not sure that I understand what you mean.

Chairman WYDEN. I was under the impression that there were some agreements that you were not to talk or something like that?

Ms. SMITH. Oh, yes. They asked me if I could please keep this completely quiet. They wanted me to sign something. I of course refused to.

In fact, I am very glad that I did not because I feel very privileged to be here. I want to help with this, and I am glad that I have the opportunity to be here because something really does need to be done.

We need some help because if something is not done, many more people are going to get sick. In fact, people are getting sick every day. I really want to see something done.

[Ms. Smith's statement may be found in the appendix.]

Chairman WYDEN. Let me just thank you for being here. I think your courage and willingness to speak out makes it a bit more likely that we will be able to get the kind of oversight that is going to be needed.

I will have some questions in a moment when we have gone on and heard from Ms. Khatami. We will have some questions of you and the other witnesses.

Let's go at this point to you, Ms. Khatami. We welcome you. You two are a long way from home. We will make your comments part of the record, and look forward to your oral presentation.

Ms. **Khatami**. Thank you, Mr. Chairman.

## TESTIMONY OF EDITH KHATAMI, COSMETOLOGIST, SAN FRANCISCO, CA

Ms. **Khatami**. Good morning to all of you. My name is Edith Khatami.

Chairman **Wyden**. Ms. Khatami, I am sorry. Let me get you to get right in front of that microphone.

Ms. **Khatami**. Oh, OK.

Chairman **Wyden**. Great.

Ms. **Khatami**. I immigrated to the United States in 1972 from Vienna, Austria, with my two children. In 1981, when my children were older, I began to look for work. Because of my background as cosmetologist in Europe, I answered an ad by Loral Wigs boutique shop looking for a stylist in Cupertino, CA.

I was hired, and I began to work at Loral Wigs in 1982. My job consisted of servicing wigs, including cutting, styling, washing, of both human and synthetic wigs, and selling these wigs to the public.

My wigs were bought by cancer patients from Stanford Hospital who came to me to do the wigs for them.

Before I started my work at Loral, I was very healthy and I had no problems. There was a small back room in which we did the wigs. In the front there were three chairs for ladies and one for men.

I spent a lot of time working on the wigs, and in that small back room. In addition to cutting the wigs, we styled them by using hairsprays called "Streaks 'n Tips" and "La Charme," which I am told contains methylene chloride, the kind consumers use.

The area in which we did the washing, cutting, conditioning, spraying, styling of the wigs was very poorly ventilated. There was no air conditioning to help circulate the air.

We had our lunch in the same room during the day. In 1984, 2 years after I began at Loral, I started to feel nauseous, dizzy, and started having vision problems.

My coworker, Carol Guerroro, had some of the exact same symptoms. She felt very nauseous, dizzy, and in fact she said she couldn't wait on customers anymore because she had become disoriented, and had trouble counting the money.

Both myself and Carol had chest pains, and feeling like we could not breathe. There was numbness and tingling in our extremities as well.

What finally made us alarmed about our health was that Carol fell outside the shop. She was feeling incredibly confused and disoriented when this happened.

We decided to see a doctor. We both asked what happened to us in this little shop. We were healthy, and now we are not.

I got referred to Stanford Hospital, and then to Santa Clara Valley Medical Center, and then to Dr. Jim Cone.

They diagnosed me as having a central nervous system disorder called cognitive dysfunction, and also occupational asthma caused by the methylene chloride wig and hair sprays I was using.

But nobody told me and nobody warned me or instructed me concerning the products we were using.

In October 1985, I left my job and I have not been able to work since then, part of the problem being now that I cannot remember things that I did just a short while ago.

That is one of the health effects of the neural toxins I was exposed to. I have to write everything down. How can I go to an employer and ask him to hire me when I do not have memory.

But I am the lucky one. My friend Carol can barely do most easy tasks because she has barely any memory function. She needs help in her house. She cannot cook because she forgets to turn off the oven. She often forgets if she has eaten. She has a cane. She has a hard time keeping the balance. And I am just using a cane occasionally.

No one ever warned me that the chemicals I was using may be harmful to me. I cannot believe the difference it has now made in my life.

It has been really hard, and the most horrible part of it all is that I know I will always have this condition.

I know from going to stores that other hair sprays have methylene chloride. I was shocked to find out that over 2 years ago, the Government proposed a ban on methylene chloride because it causes cancer, but has never done anything about it.

How many more people have to get sick before the Government does something about it? It is not fair. It is not right. If the Government does not care, who will?

Thank you, Mr. Chairman, for giving me the opportunity to speak.

[Ms. Khatami's statement may be found in the appendix.]

Chairman Wyden. Thank you very much, Ms. Khatami. All of you have been excellent in your presentation. And let me, if I might, start with you, Ms. Smith, with some questions.

Tell us, if you will, a little bit about the work environment there at your school. Were the fumes just everywhere, and overpowering on a daily basis?

Ms. Smith. There was constantly things being sprayed. There was constantly perms going on at all times. There was no ventilation at all. It was just one big room with so much of the chemicals around it at all times.

Chairman Wyden. What kind of fumes were used primarily? Were these hairsprays, sculpturing nail——

Ms. Smith. Hairspray was used constantly. We worked on older women with the beehive-type hairdos that require a lot of hairspray. So there was constantly hairspray being sprayed. There was constantly perms going on.

Chairman Wyden. Sculptured nails, I gather——

Ms. Smith. There were nails going on. Nails that—those fumes are just, you know, they would make you sick if you were—I mean

I can see how they would make somebody sick that does them all the time.

If you were just getting them done, you could get sick. They are really strong.

Chairman WYDEN. As you found yourself with these health problems, did you tell your instructors about this?

Ms. SMITH. Yes; I did.

Chairman WYDEN. What was the response of your instructors?

Ms. SMITH. They just told me that—to quit complaining about it. I tried to explain to them how I was feeling. But obviously, they did not care. They were not real concerned with what I was trying to express to them.

Chairman WYDEN. Were the bottles that were used at your school of the nature that Ms. Shulman described? Ms. Shulman made the point which I find very frightening, that at least there is some information on products you might get in a retail store. But particularly, some of the workers in the salons use these clear bottles—bottles with no ingredients on them at all.

Were those the kind of bottles that were used in your program?

Ms. SMITH. Yes; there are no instructions—there are no ingredients on them, there are no warning labels of any kind. So we were not aware at all that there could be a potential problem with them.

Chairman WYDEN. Were there any manufacturers labels on——

Ms. SMITH. Yes; on the permanent bottles, we never did see them. If we had a patron come in, and we were told to do a perm—we asked the instructor if they would get it for us, and they would go to a cabinet and give a couple of bottles that were completely unmarked.

Chairman WYDEN. Did anybody at any point through your training tell you that there might be health risks posed by any of the products that you were working with?

Ms. SMITH. No; they told us a little bit about hair colors. But in general, we were completely unaware of the health hazards.

Chairman WYDEN. When you worked with these products—at least initially—did you just assume that somebody had approved them, somebody in Government, as being safe?

Ms. SMITH. Yes; you kind of would think something as strong as a chemical—I mean a chemical is like a drug. You would think that we were safe. I had no idea that these things were not approved at the time.

Chairman WYDEN. What about the long-term health effects for you? I gather that this has been a condition that makes it hard for you to do some of the things you would like to do as an employee. Are there other problems that you may face, long-term health kind of problems?

Ms. SMITH. Other than the breathing are there health problems? I do not think they are health problems. They are just mentally very distressing for me.

When I am having the attacks, I can still function. I cannot do—I feel very tired all the time. It is hard for me to work. I have to continue working all the time.

But when I am on medication, I just feel very drained all the time. More than anything, I get so upset because I just want to be able to breathe.

Sometimes when I am able to get my breath, I mean I will try like 10 times to get it, and when I finally get it sometimes I smile because I am so happy that I finally got it.

Chairman WYDEN. How often do you have these breathing attacks, Ms. Smith?

Ms. SMITH. It is really—it can happen every other week. It can happen—I will be fine 1 day, or 1 hour, and the next hour I will have it.

It is continual. I just got over one that lasted a month. That was one of the worst ones I have had in a while. So I have been over it for about a week. Like I said, I appreciate breathing so much.

Chairman WYDEN. Are they getting worse over time?

Ms. SMITH. They are not as bad as they were when I was in beauty college. But they are still bad enough where it completely affects my life.

Chairman WYDEN. During this month period where you had a recent attack, did that severely limit your activity? Did it make it difficult for you to do things that you might otherwise do

Ms. SMITH. I just want to lay down all the time. Being around other people, there is a major change in my personality. I am just so upset at all times from it that it completely effects my everyday life.

Chairman WYDEN. The only other question I have at this point is I understood you to say that you are now given additional drugs to deal with your asthma problem, is that right?

Ms. SMITH. Additional?

Chairman WYDEN. Yes; I mean because of the asthma condition you now have to take other medicines to treat the asthma.

Ms. SMITH. Yes; I take medication daily. I have to take Theoclear twice a day when I have real bad attacks, I take something called cretizone. It is very strong. It has some strange effects, but it helps my asthma.

Chairman WYDEN. Are those steroids?

Ms. SMITH. Yes; they are.

Chairman WYDEN. So there are other health effects that you may face as a result of these problems.

Ms. SMITH. It is like——

Chairman WYDEN. The domino effect.

Ms. SMITH [continuing]. You do not know would you rather breathe, or would you rather feel bad from taking the drug. So it is——

Mr. WYDEN. I again just want you to know how much I appreciate your being here. And I know this has been hard for you.

Chairman WYDEN. Really, the only reason we have asked you to come is because we think this gives us a chance to get some of the reforms that are going to make it more likely that other Americans will not face the kind of problems that you have, and want to thank you——

Ms. SMITH. Thank you very much. I am very glad to be here.

Chairman WYDEN. Ms. Khatami, let me move to you.

Did your employer ever alert you to the danger of inhaling the fumes in the shop or——

Ms. KHATAMI. No.

Chairman WYDEN [continuing]. Any health risks?

Ms. KHATAMI. No.

Chairman WYDEN. What were the first symptoms you had from exposure to the substances in your shop?

Ms. KHATAMI. I was very dizzy, very nauseated. I had terrible headaches, extremely terrible headaches. I could not breathe. I had difficulty breathing. In this particular shop, there was only one door to enter and exit. No windows. No attic or air conditioning.

Chairman WYDEN. How soon after you went to work there did you begin to experience some of these health problems?

Ms. KHATAMI. I started with a little headache, I think, after 6 months. But after 2 years, I really got severely ill—I could not breathe.

I had terrible cramps around my heart. I could not breathe. I was nauseated, very dizzy. Finally in 1984, I began to see doctors. We actually really could not find out what it really was until I went to Stanford, and Stanford referred me to occupational health center in San Francisco and San Jose.

Chairman WYDEN. Now you testified that you had trouble with your memory. Has that——

Ms. KHATAMI. Yes; very much so.

Chairman WYDEN [continuing]. Effected your life and your employability, and things of that nature?

Ms. KHATAMI. Very much so.

Chairman WYDEN. How so?

Ms. KHATAMI. I cannot remember—I even forget sometimes to turn the oven off. So I have to check three, four times. Have to check all my clothes—my keys, I close my house. This is all right.

Now I also have difficulties walking. I have extremely pains in my fingers, in my arms, my legs.

Chairman WYDEN. You have those problems on an on-going basis?

Ms. KHATAMI. Yes; you never can say, the breathing, how it is going to attack you, how long it is going to take, when it is going to come, when you are going to have the pain. You do not know.

Just one day you feel good. The next day you are so tired you cannot do anything. Mostly what is bothering me is the memory. It is very hard to communicate.

Chairman WYDEN. Tell me, if you will, about a typical day at your shop. I gather that you were involved spraying wigs, and there are heavy fumes associated with that?

Ms. KHATAMI. I sprayed about 8 hours—8 to 9 hours a day. Sometimes I worked 7 days a week. I actually lived in that shop. I mean, I did not live there but my whole working was mostly in that shop.

Chairman WYDEN. Did you at that time think that the Government had approved the use of these products, or that someone had taken steps to assure that they were safe?

Ms. KHATAMI. I assumed they were safe. At that time we did not know.

Chairman WYDEN. Are you surprised that chemicals like methylene chloride, the solvent that can cause central nervous system effects such as you are facing are allowed into these products?

Ms. KHATAMI. No; I am not surprised, no.

Chairman WYDEN. What about the ventilation where you worked? Was that a problem as well?

Ms. KHATAMI. Very poorly. Very poorly ventilated.

Chairman WYDEN. So the situation is you are there spraying 8 hours a day——

Ms. KHATAMI. Right.

Chairman WYDEN [continuing]. In a poorly ventilated place. And shortly after you begin to do it you begin to experience these health problems?

Ms. KHATAMI. Right.

Chairman WYDEN. I want to thank you as well, Ms. Khatami. You have been very helpful. We are looking forward to working with you in the effort to bring about some reforms.

A few questions for you, if I might, Ms. Shulman. I say only a few because you gave such very good testimony.

Are we facing isolated cases? Are the kind of cases that we heard from Ms. Smith and Ms. Khatami—these are aberrations, or these just unusual kinds of things? You hear from people in your union all around the country.

I mean just how serious and how widespread is this in your opinion?

Ms. SHULMAN. I wish I could state that the cases you have heard this morning are isolated cases. But the fact is that the health problems experienced by Edith Khatami and Kristi Smith are just an example of the myriads of problems I have seen travelling around the country and hearing from letters that members and workers in this industry have sent to me.

This is a problem that is happening everywhere in the United States, not just the two women here. And as you have heard this morning, there are serious problems.

We are talking about asthma and neurological problems. Also, obviously, skin problems that are a result of some of the chemicals that they are using in the salons. But this is a widespread problem that needs to be addressed.

Chairman WYDEN. In your view it is not one that is just a matter of individual sensitivity by a small number of people, or some who are allergic to certain ingredients, or something like that, but something much more widespread?

Ms. SHULMAN. This is very widespread. It is not a question that there are a few people who are hypersensitive to certain chemicals.

We are finding that lots of people in this industry—in other words, people who just go to work in this industry are having this problems.

The problems also that you have heard this morning of poor ventilation, lack of education in terms of using the products, is absolutely spread throughout the country.

There is no education as to the products. There is no addressing of the widespread problems in terms of the health effects of cosmetics.

Chairman WYDEN. What has been the response of the Food and Drug Administration and other Government agencies when you take to them your concerns about illnesses and injuries to your members?

Ms. SHULMAN. We sent a letter to the Food and Drug Administration. The response to that letter is on the—attached to the testimony I have submitted this morning.

The problem is the FDA says over and over and over again whenever we call them, we do not have the authority—we do not have the authority, Ms. Shulman, we cannot do anything about it.

We do not have the authority to pretest. We do not have the authority to get the manufacturers to submit ingredients. We do not have the authority to get the customer complaints. We just do not have the authority.

Chairman **Wyden**. Is it your position that Congress should alter the Food Drug and Cosmetic Act to give the Agency the authority to do those kinds of things?

Ms. **Shulman**. Absolutely; unless we have legislation to mandate the kinds of protections we are talking about, nothing will occur in terms of making sure that workers and the consumers are safe.

Chairman **Wyden**. Are steps being taken by Government to document the extent of the problem? Are records kept, or things of that nature?

Ms. **Shulman**. The catch-22 is there is no requirement for manufacturers to submit customers' complaints and consumer complaints. So there is no way of documenting the problems in terms of consumers throughout this country.

Chairman **Wyden**. What about the question of testing—testing on people to see if there are long-term effects from exposure to products. Are there these kinds of tests?

Ms. **Shulman**. There is no requirement that these tests be made before they come on the market. So we have no way of knowing whether they are safe when they come on the market. We have no way of knowing this.

Chairman **Wyden**. So OSHA is really taking no steps to deal with these matters?

Ms. **Shulman**. OSHA defers to the FDA and says this is their jurisdiction. FDA says that they have no authority pursuant to legislation.

So we are, in a sense, in a tremendous loophole of regulation where there is nothing being done by any Federal agency.

Chairman **Wyden**. Supposing I go home tonight, OK? I go home tonight instead of playing basketball with my little boy, or something like that, I throw a few ingredients together, I put them in a package and call it hair dye, or antiaging cream, or something like that. Can I do that?

Ms. **Shulman** The great irony is that Herb Dennenberg, a TV anchorman, did a series doing just that. What he did is he came up with a cream, packaged it, put anything he wanted into it because it does not have to be tested, does not have to be labelled, nothing has to be done, and pawned it off to salons around Philadelphia. They bought it. It was on the market.

I mean it is scary, truly scary to think that that can happen, that a product like that can be used by workers and consumers.

Chairman **Wyden**. If I go out and do this, and I suddenly give it to a small shop, or something like that, there is not any labelling.

Ms. **Shulman**. There is no requirement that it be labelled if it is just used in the salon.

Chairman **Wyden**. What is the range of products we are talking about here—hair dyes and a variety of nail care, a variety of products I guess we have already talked about. But how many products are we talking about?

Ms. **Shulman**. We are talking about thousands of products. We are talking about everything when we talk about cosmetics. It can be shampoos. It can be toothpaste. It can be deodorant. It can be hairsprays, hair dyes, perm solutions; anything you put on your face in terms of hair creams, mascara, lipsticks—anything you can think of that we use on our bodies.

Chairman **Wyden**. Let me ask you what I think is an important question with respect to regulation because always, what we want to do is look at the least cumbersome, least burdensome, least restrictive way to address health care kinds of questions. Certainly one is looking for voluntary approaches if one possibly can find it.

Have you all ever asked industry on a voluntary basis—apart from any congressional FDA-OSHA kind of action—have you all ever asked industry to voluntarily label products that are used in these salons?

Ms. **Shulman**. Absolutely; we, like you, believe that the least amount of regulation is always the better, if industry would take the responsibility to do what they are supposed to do in terms of protecting workers and the consuming public. We asked the manufacturers to voluntarily label, and they refused.

Chairman **Wyden**. Ms. Shulman, I think that is an important point. I want to assure you that I am certainly going to push for this kind of information to be made voluntarily.

I mean, that just seems to me to be a modest kind of step. One can debate Government proposals, and I suspect we will. But it would seem to me at the very least people ought to have a little bit of basic information when they use these products.

Now you said the manufacturers do not have to tell the Food and Drug Administration about consumer complaints that they received?

Ms. **Shulman**. That is correct, Mr. Chairman.

Chairman **Wyden**. Well, how does Government hear about complaints? I mean, I would assume that consumers first go to companies. But how does that information even get passed up?

Ms. **Shulman**. It is unknown to me. In other words, it can be kind of anecdotal in the sense that maybe somebody finds their way to the FDA and lodges some complaint.

But the sad part of it is that there is no collection of data so that we can really understand the long-term health effects of these problems because the FDA is not required to collect this data.

Chairman **Wyden**. I have just one other question. Then I want to recognize my good friend from New York.

What you have really said is that the present system is hit and miss. If the Government is going to hear about it, it is going to come about as a result more by accident than anything else.

Ms. **Shulman**. Absolutely; before I close, Mr. Chairman, I would like to introduce one person who is instrumental in these hearings, Debbie Berkowitz, to my right, who is the director of health and safety for the Food and Allied Services Trade.

Ms. **Berkowitz**. Can I just say one thing that I just want to clear up? That is, we are not saying that the cosmetic industry puts products on the market and does not do safety testing.

They would be crazy not to, and they have to do something. But what we are saying is, who is doing the long-term testing? How do we know that they are doing it? What kinds of tests are they doing?

There is no standard that defines what is safe for cosmetic products, like there are for other products.

Chairman **Wyden**. That is a very good point. I appreciate your making it clearly. I want to recognize the gentleman from New York.

Mr. **Flake**. Thank you very much.

Mr. Chairman, first of all, I want to thank you for holding this hearing, and those who have come to share information with us this morning.

Ms. Shulman, I'd like to ask a question of the chairman which has to do with regulation. One of the concerns I have is if we are to try to create the mechanism by which products are to be tested—and one thing that comes out clearly from both statements is that they were functioning in environments that were poorly ventilated and that were not meeting the highest available standards—then it seems to me that we must create the same kind of environment. If we are going to talk about regulation, we must extend beyond the actual product, and deal with some standard by which shops must operate under. Would just like to hear your comments on that.

Ms. **Shulman**. Congressman Flake, you have addressed a very important issue. Salons throughout the United States are poorly ventilated.

What you have heard today is what is really widespread. Part of the problem is that there has been no education in terms of the fact that there needs to be better ventilation in these salons.

So we would have to address the fact that there needs to be the kind of ventilation to make sure that these chemicals—basically, there is not as severe an impact of these chemicals.

So we would have to clearly look at the kinds of ventilation which is necessary as well.

Mr. **Flake**. Is there currently a requirement in the industry for persons who are either entering the training schools or moving into the industry to take any kind of health examination before entering?

Ms. **Shulman**. It is my understanding that there is no requirement. Additionally, the problem is that when you look at the curriculum of the beauty schools, of the barber schools, there is virtually nothing being taught in terms of the impact of all these chemicals.

So no one knows that they should look at their salon, in terms of ventilation, no one knows that really they should use certain kinds of gloves with regard to certain perm solutions, for example.

No one understands that there are problems out there that they can at least do minimal things to prevent, or at least lessen the effect of these.

Mr. **Flake**. I am going to assume that in most municipalities, the health department takes some responsibility for assuring a relative amount of health standards within a shop.

Beyond whatever the health department does, though, is there any other agency or department that your group would like to see involved in the process of trying to change the general working environment?

Ms. **Shulman**. We would always welcome any agency in terms of making sure that the environment in working places are safe. Problem is, if we call in OSHA, which we have tried to do in various situations, they come into the salon, they look around, and they ask, what are you using.

They look down at the ingredients, and there are none on the label. So they cannot test if they do not know what is in it in terms of the levels.

More importantly, OSHA can just look at the levels that these things are at in terms of the salon. These things are being applied to your body, and put into your bloodstream. That is something they can't calculate.

Mr. **Flake**. In a shop where the atmospheric conditions are in many ways determined by the number of different products that are being used, and as the chemicals begin to mix with each other, obviously we have the potential for consumers being affected as well.

Is there is no process at this time for measuring those atmospheric conditions?

Ms. **Shulman**. Well, they can measure, you know, certain levels of what is in there. But they do not know what is in there. That is the problem—one of the problems.

You have also made a very important point in terms of just the consumers. The consumer sits down to have their hair dyed, or hair permed, or just have their hair cut using none of these products.

They are sitting in an atmosphere where there is all of these chemicals mixing together. We have no idea what the short-term or long-term effects of those mixed chemicals will be on consumers.

Mr. **Flake**. Thank you very much.

Ms. **Shulman**. Thank you.

Chairman **Wyden**. Just one other question, perhaps for you, Ms. Shulman. I gather that OSHA now has, or is working on a hazard communication standard that could cover beauty shops, and barbershops, and things of this nature.

Is this going to help your workers? If not, why not? If so, why so?

Ms. **Shulman**. The problem with the hazard communication standard, first of all, it has been stayed as of today. But even, let's assume that it goes into effect, the problem is that they get something called material safety data sheets. As this subcommittee looks at small businesses, you really understand the problem. To get material safety data sheets from the manufacturers to the distributors, to the distributors to the owners, to the owners to the workers, we are talking about these sheets being lost somewhere halfway between all these various steps along the way.

The easiest way, and it seems to me the most rational way of dealing with these problems in terms of just knowing what is in them is, one, labeling.

It just makes the most sense. It is the most direct. You can look down at whatever it is in terms of your ingredient. We applaud the hazard communication standard. But obviously, it makes most sense if you'll just be able to look down at your product and know what's in it.

Chairman WYDEN. Let me ask you a specific question on that ingredient situation. The agency cannot ask for ingredient information now from the manufacturers as it relates to the specific way the product is formulated, is that right?

Ms. SHULMAN. That is correct.

Chairman WYDEN. OK, and that is in particular what you would like today?

Ms. SHULMAN. Absolutely; we would like to see the requirement having ingredient formulations submitted to the Government, as well the consumer complaints and test data as well.

Chairman WYDEN. Because without it, you cannot really understand what the product is about.

Ms. SHULMAN. There is no way of knowing.

Chairman WYDEN. You can get some information about ingredients, but you cannot really understand how these ingredients work in combination, and essentially how the product really will affect people.

Ms. SHULMAN. That's true.

Chairman WYDEN. You all have been just exceptionally helpful. I want to thank you for your patience. We will be in touch with you probably often in the days ahead.

Ms. Smith, in particular, you came an awfully long way from home. I want to thank you for doing so. If you have nothing further we will excuse you at this time.

Ms. SHULMAN. Thank you, Mr. Chairman.

Chairman WYDEN. Thank you all.

Our next panel will be Ronald A. Karp, an attorney with Chaikin & Karp, Washington, DC.; Dr. James Cone, director of Occupational Health Clinic, San Francisco General Hospital, San Francisco, CA. If you all will come forward.

Dr. Karp.

Mr. KARP. I'm Ronald Karp.

Chairman WYDEN. Excuse me. Ronald Karp, Dr. Cone, we welcome both of you. Let me just ask our guests in the interest of time if those of you would like to visit please do so outside the hearing room cause we are going to have to move on.

Gentlemen, it is a practice of our subcommittee to swear all witnesses before the subcommittee. Do either of you have any objection to being sworn?

A VOICE. None.

Chairman WYDEN. Please rise and raise your right hand.

[Witnesses sworn, en banc.]

Chairman WYDEN. Gentlemen, we will make a copy of your prepared remarks a part of the record in their entirety. Let us begin with you, Mr. Karp.

## TESTIMONY OF RONALD A. KARP, ATTORNEY, CHAIKIN & KARP, WASHINGTON, DC

Mr. KARP. Mr. Chairman, members of the subcommittee, my name is Ronald Karp. I am a partner in the firm of Chaikin & Karp in Washington, DC.

I am past president of the Trial Lawyers Association of metropolitan Washington, currently, I am the District of Columbia delegate to the American Trial Lawyers Association.

I recently had the task of trying a case in the Federal court in Baltimore which resulted in the $450,000 verdict for a woman whose hair caught fire as a result of using a popular hair product.

That verdict has just been upheld by the United States Court of Appeals for the 4th Circuit. During the course of this litigation, and particularly, after the verdict which was reported in the media and legal journals, I began hearing from lawyers all over the country with similar cases.

Black women are using hair products designed to give them the popular Jeri-Curl and they are having their hair catch on fire and suffer severe burns.

In my case, Laverne Greene, age 42, used the product on the evening of December 21, 1985. She covered her head and went to sleep.

The next morning she was alone driving in a car when she struck a match to light a cigarette. A spark flew to her hair, and she heard popping and cracking noises.

Her head had become a human torch. She tried to pat out the fire, and it now spread to the roof of her car.

She got out of her car, and two men seeing her in distress reached over and managed to eventually extinguish the flames.

She was hospitalized for 4 weeks with severe burns. Her eyes were swollen shut, and she underwent painful burn treatment including skin grafts.

Mr. Chairman, I brought just a few pictures of Ms. Green and what she looked like when the brought her to the hospital. I think it is fair to say that these photographs are unbelievable.

We were led to believe at first——

Chairman **Wyden**. Without objection, we will make them a part of the record as well.

[The photographs referred to may be found in the subcommittee's files.]

Mr. **Karp**. Very well. Thank you. We were first led to believe, Mr. Chairman, by the company that this incident was a fluke; that there was no relationship between the hair fire and the hair products.

The court ordered the company to produce complaints of fire incidents, which we had been trying to get, and which they said were irrelevant.

We found out that this incident was not a fluke at all. It had happened before.

We had tests performed at the Worcester Polytech Institute in Massachusetts by Professor Richard Custer, who was formally with the National Bureau of Standards, and is a specialist in fire safety prevention.

Professor Custer testified that the chemicals used in these hair products caused a grease fire, and this grease fire occurs when it is ignited by a match, or any other source of ignition.

Normal, untreated hair could be extinguished by patting it out. But hair treated with the Jeri-Curl products cannot be readily extinguished.

Indeed, when Laverne Green tried to pat out the grease fire her hands—the palms of her hands became extremely burned as well.

As I have said I since heard from lawyers all over the country who have related to me tragic, similar incidents caused by a variety of hair products, not necessarily by the same company, but by a multitude of companies all marketed to predominately black females who want a Jeri-Curl.

As we speak right now, I have no doubt that thousands, perhaps millions of women have these products on their hair without any understanding of the danger they may suffer if their hair comes into contact with a spark or any other source of ignition.

Some of these products carry a warning which states, "Keep hair away from open flames." We had a human factors expert testify at trial, one Dr. Robert Cunitz, also formerly with the National Bureau of Standards.

Dr. Cunitz testified that this kind of warning is wholly insufficient to adequately notify the consumer of the risks involved in using these hair products.

He pointed out that the warning does not tell one how long one must stay away from open flames, or why one must stay away from open flames, or whether matches or smoking can cause a special hazard.

He felt that the warning was not adequately displayed, and fundamentally that the products were too dangerous to be on the market in their current state.

There are various companies that market the Jeri-Curl, and some of the products have no warnings at all.

I went to a drug store last night and picked up several of these products. They all contain such chemicals as glycerine and propylene glycol, the residue of which causes a grease fire when ignited.

Women who are buying these products ought to be warned of the risks involved in using them so that they can make an informed choice.

They ought to be explicitly told that smoking around these products can be more than hazardous to your health.

When hair containing these products is ignited, one's life can change forever because the scarring is permanent, the burns so deep that no new hair will grow.

The sweat glands are destroyed, and going out in the sun is prohibited. As I speak to you now, my client, Laverne Green is sitting in her apartment.

She cannot go out in the sun, even with her head covered, without experiencing pain. She cannot go to the supermarket without people staring at her head because the burns are all over her ears and she has to have extensive covering on her head.

She is a prisoner in her own apartment, as are many burn patients, but these burns could have been easily prevented.

I have been told of similar tragedies involving teenagers who use Jeri-Curl products. What will happen to their futures? What will happen to these young girls who are permanently scarred?

All of this is too high a price to pay for inadequate warnings. I would like to point out, Mr. Chairman, that the testimony in our trial was that it only cost a few pennies to put an adequate warning on the project.

It seems to me in summation that if we can force cigarette manufacturers to put warnings on cigarette packs that tell consumers they may get cancer years in the future, we can force cosmetic manufacturers to wan women that their heads may turn into human torches tomorrow morning. Thank you.

[Mr. Karp's statement may be found in the appendix.]

Chairman **Wyden**. Thank you very much, Mr. Karp. I looked at those pictures. It is just beyond belief. Thank you for coming.

Dr. Cone, we welcome you. We look forward to your oral presentation.

## TESTIMONY OF JAMES E. CONE, M.D., M.P.H., DIRECTOR, OCCUPATIONAL HEALTH CLINIC, SAN FRANCISCO GENERAL HOSPITAL, SAN FRANCISCO, CA

Dr. **Cone**. Mr. Chairman and members of the subcommittee. My name is James Cone. I am a medical physician with a masters degree in public health.

I am currently chief of the Occupational Health Clinic at the San Francisco General Hospital, and assistant clinical professor at the School of Medicine at the University of California in San Francisco.

We are part of the Northern California Occupational Health Center, a multidisciplinary training, service, and research center which, since 1979 provides consultations for industry, union and medical practitioners, as well as government agencies regarding potential health effects of work and the environment.

I want to emphasize that we are a referral center. Thus we only see the tip of the iceberg in any specific area.

We see patients who have been referred by their regular physicians in the emergency rooms, or in the community who have been puzzled, or unable to make the association properly between exposure in a salon, for example, and the dermatitis, the neurological problem, or as we have heard, the asthma problem.

This is not an easy association to make at times. Therefore, we are asked to provide this service.

I am pleased to be here today to discuss four cases, which I believe illustrate some of the problems which face a large number of cosmetologists and hair dressers in this country, as well as, we have heard, some consumers.

There is a general lack of awareness of the potential health problems due to cosmetics, which I believe is made worse by the failure to warn on the part of manufacturers.

I would like to present four cases, briefly, and I will be glad to respond to questions after that.

The first case is very similar to the type of problem reported by Kristi Smith, first case that we heard this morning. We saw a 36-year-old female cosmetologist who had a prior history of asthma, as approximately 5 percent of the general population does, which was well-controlled. She had no need for medications other than she had occasional seasonal allergies that made her asthma worse, until she went to beauty school and then began working as a cosmetologist.

She was able to work as a cosmetologist for several years without significant problems, until she began working in a salon in the middle of a large department store.

You probably have been by these types of salons. They have closed doors. The closed doors suggest that the workers and other people in the area are perhaps bothered by the fumes from the salon.

Therefore they are fairly tightly closed up. That I think is unfortunately an all too common factor—lack of ventilation has been pointed out as a major contributing factor.

After several months working in the salon she developed increasing wheezing, which began at about 10 in the morning, then progressed during the day to the point where she had to go to the emergency room of a local hospital.

She began to take more and more medicines, including steroids. Despite these medications she continued to have worsening of her symptoms to the point she consulted another physician at an allergy clinic, asking, "What is causing this? I don't understand."

She was tested. But again, lack of information about what exactly she was exposed to made it difficult for the allergy physician to even know what to test for.

She finally consulted the Occupational Health Clinic when she began to really suspect some occupational cause. Often the patients go for years without even having a suspicion of an occupational cause.

When there is no suspicion, it is hard for them to communicate with their physician that there may be a clue in their work.

They had never been told that many of these products contained potential irritants or allergic sensitizers. We performed a careful evaluation including having one of our trainees go out and inspect the work site, which we also provide as a service.

The patient remarked that air filters were present but were stopped up. According to her, they were never maintained properly. Labels were absent for many of the professional hair care products, as we have heard. Commercial hair care products, for some reason, have escaped the labelling requirement that is present on consumer products.

We did find some manufacturers had provided material safety data sheets for some of the products, which have been mentioned as a potential back-up means of finding out what the chemicals are.

California OSHA, prior to its demise, required material safety data sheets. Unfortunately, that regulation has not been enforced effectively in all shops. Many of these products have simply other ingredients listed on the material safety data sheet. That is hardly an adequate description of the contents.

Due to these multiple problems, we were unable to identify which of the many compounds she was exposed to which may have caused her problem.

We recommended that she actually be removed from work. That is, again, as we have heard, a serious blow to a person's future professional career.

She has now been away from further exposure and has 75 percent improvement in her symptoms. She is able to continue without daily medication, almost back to where she was prior to her work in the cosmetology industry.

But I think this illustrates a fact that many of the workers in the country have underlying medical problems which normally would not cause anybody a problem.

People with asthma are working today in many, many small businesses throughout the country without problems. It is only when they are exposed, unknowingly, to something that can increase their symptoms that it becomes a work problem.

It would not have to develop into a work problem if workers were properly warned and there was proper ventilation.

The second case, very briefly, is that of a skin problem. We have heard mostly about the neurological and respiratory problems. The skin problems are really the most common thing we see in the hair products industry work force.

A 42-year-old beautician developed first some symptoms of nausea, difficulty with aching in her legs, and headache. But then in one episode, she was unloading some materials from a store room. One of the bottles was broken. She noted the odors very strongly in the air, and became very dizzy and had difficulty breathing, actually fell off the stool, bruised her back and ankle, and had to go home because she was feeling so overwhelmed by these fumes.

She then noted skin problems. These were typical hives with itching and large blotches. These covered her body, mainly her arms and her head. She went to an emergency room. They asked her what it was she was exposed to.

She told them she was exposed to a particular product but she did not have the name of any specific chemicals on the label.

She was told that she was probably having something called chemical urticaria. This is the technical name for hives induced by chemical exposure.

She was treated with proper medicines, and she tried to return to work despite their advice to avoid further exposure. She tried to return on repeated occasions, she was determined to do so as this was her career. She wanted to try to go back to work as best she could.

However, every time she went in, any time there was a tint or a permanent wave process going on she developed severe difficulty breathing and these hives spread throughout her skin, to the point where she would have to leave to go to the emergency room.

She once required injections with epinephrine, which is a treatment for anaphylaxis, a bodily response to exposure to something which you are very allergic to, similar to some peoples' response to a bee sting.

She had a similar reaction to just walking into a salon. At that time we were unable to find out what exactly the name of the product or the constituents were to be able to even tell her what she should avoid that may provoke this life threatening response.

We advised her to leave the industry. She is required to have vocational rehabilitation because really she is at risk of very serious injury if she is exposed to whatever this particular cause of her problem is.

The third case is, again, one of the common types of problems mentioned by Beth Shulman earlier, that of a beauty school using nail care products. Here the products not only affected the people in the beauty school, but as is unfortunately common, they were taken home.

Taking products home and practicing on themselves or their family may lead to potential exposures to family members, children, and the community.

In this case, a baby who happened to be in the home at the time developed symptoms of bloody nose, red throat, and red eyes at the same time this student was trying to learn how to do the work of her trade.

This is normally performed in a school with 100 students all doing the same type of work in a large room, as we have heard, unventilated, except for two fans, one at each end.

No gloves, unfortunately, or respiratory protection was provided.

We contacted the school. We were very concerned that other students may have been affected.

In fact, they reported four other students that had very similar responses—nose bleeds and very severe upper-respiratory irritation.

The owner said they were so concerned they called the manufacturer. The manufacturer became concerned when they heard the numbers involved, and recalled the product from that school.

The school then switched to a different product, and has had less problems since then. However, this case illustrates the problems of an unregulated industry again.

You have products going into use on a wide scale without really adequate testing. They then are tested on the students, in fact, who become the guinea pigs. Then once there is an effect the product is recalled, but there is really no guarantee that other schools or other persons using that same material would have had a similar recall so that they may have been protected.

It is admirable that the company recalled the product. But I think there needs to be some public health protection to make sure that that is not just simply from that school alone.

The last case, I think, is just a very brief confirmation of what we have heard from Edith Khatami. I was the physician that saw Ms. Khatami in consultation. A colleague of mine also saw Ms. Khatami's coworker in the same wig shop.

I was frankly shocked by the degree of impairment that we saw in these two workers. It was really an eye-opener for me to see that a product which we would expect to have been tested and proved to be safe could cause as severe a problem as we have seen in these two individuals.

Partly as a result of these two cases, we have actually embarked on a research study looking at health effects of methylene chloride in other workers who have been exposed, perhaps maybe not as intensively as these two workers. But this is a problem that has not been adequately studied in general in the work place. And we certainly look forward to completing that study.

Finally, I would like to summarize. I think there are some relatively inexpensive, simple ways that we can address this problem that are going to be hopefully able to prevent any further cases like we have seen today.

First is that workers in this industry need essential information. Anybody who works in the chemical environment needs to know what they are working with, and labelling of professional products, I think, is an essential first step.

To avoid confusing cosmetologists with long chemical names that may not mean too much to a nonchemist, I think we need to also address the issue of how to put some information about what the health effects are on the label as well.

Simply having a long name that has 15 syllables and lots of numbers in it may not be as useful to the cosmetologist having a skin problem as having something on the label as a simple symbol that there is a potential skin sensitivity.

It could be a very simple symbol. It would not have to be large. It would not have to overwhelm the label. Would simply be a clue so that when the person looks at the label they could say to their physician, yes, I am exposed to one of the ethanolamines and on the label there is a little skin sensitivity indicator that may give the physician a clue to look at that particular product, and they have an idea that the skin may be reacting to it.

Chairman WYDEN. Doctor, I know you have several other recommendations. I know they are good ones. Unfortunately, Mr. Flake and I have a vote on the floor.

If you would not mind, we will break for about 10 minutes, make the vote, and we will come back and hear your other recommendations.

Dr. CONE. OK, thank you very much.

Chairman WYDEN. Thank you.

[Recess.]

Chairman WYDEN. The subcommittee will come to order. I want to apologize to you, Dr. Cone, we had two votes in a row. I am sorry for the delay.

You had touched on your first recommendation which dealt with the labelling issue, and I know you have several others.

Why don't you proceed to give those to us?

Mr. CONE. Yes; thank you very much. I really appreciate the opportunity to address you today.

The second recommendation is that really the schools are the place where often the cosmetologists learn their trade. Really, I think it is imperative that adequate chemistry and toxicology be provided in part of the curriculum, that they are able to go out into working in the salons, and be able to know what the meaning of the label is once there is a label—that's the first step. Once there is a material safety data sheet, what does it mean? I think that is a major flaw in the concept of labelling if all you see is a long chemical name.

Students should be able to know what should be provided in terms of respiratory protection. A glove is not first a glove. There are very many different kinds of gloves. They are just very specialized for a particular product, particular chemical. Just wearing any old gloves will not protect anybody from a particular product.

Similarly, respiratory protection is not a simple matter of putting a mask on, particularly in a salon where, if you put a mask on a beautician, the customer runs out the door. The customer will likely say, "Why does this person have a mask on? I think there's a major problem here."

The workers cannot adequately protect themselves because to do so would frighten their customers.

There are not very many industries where you are working with this type of intense chemical environment which needs protection, but there is such a tremendous barrier to wearing adequate protective equipment.

The cosmetologists do not want to wear the respiratory protection because there is a potential for frightening away the very people whom they are trying to serve.

There is a need, I think, to really look at substitution. Many of the chemical industries have been tremendously innovative, have been able to come up with a tremendous variety of products.

But we need safer products to be substituted for the hazardous product. Ingredients which are known or suspected carcinogens have no place in something that is put on your skin, or put inside your body.

Strong irritants or synthesizers not only should be labelled but should be removed. Labelling is one step, but to leave them in the product and label them is not really solving the product unless people can protect themselves.

Hopefully, substitutions can be found which are less irritating, less sensitizing.

That brings us to the point of premarket testing, and not just new products. The problem is that current testing requirements are primarily aimed at new ingredients. These are things that have not been tested, a brand new product, some new chemical.

However, what really is needed is testing all the ingredients, including the old ingredients. The new combinations may be as hazardous on something new pulled off the shelf made in a new chemistry laboratory.

Finally, really to even answer this question, we need some better information. I think that is really the crux of what one of our first speakers, Beth Shulman, said: That information is missing from the FDA.

They do not have requirements for notification of actual consumer complaints or beautician complaints. There needs to be an epidemiologic approach, as well as toxicologic approach.

Not just testing animals, but to see what happens to the human guinea pigs in the work place.

So I really do thank you for the opportunity to address these important issues. And I look forward to hearing your questions.

[Mr. Cone's statement may be found in the appendix.]

Chairman WYDEN. Doctor, thank you very much. I will have some questions in a moment.

Mr. Karp, let me begin with you if I could. Could you tell the subcommittee where Ms. Green purchased this Jeri-Curl product?

Mr. KARP. She purchased it at a small beauty salon out in Maryland.

Chairman WYDEN. What cosmetic company manufactured this Jeri-Curl product?

Mr. KARP. It is called M&M Products out of Atlanta, GA.

Chairman WYDEN. M&M Products from Atlanta, GA.

Mr. KARP. Not the same makers of M&M candies.

Chairman WYDEN. Right; is that a subsidiary of a bigger company?

Mr. KARP. I do not think so. It is a major company. It is a multimillion dollar company.

Chairman WYDEN. Do you know what is the dollar volume of the company's sales for this Jeri-Curl product?

Mr. KARP. I really do not. But I remember during the course of the trial we ran across a magazine article that listed the top 100 black enterprises in America, and this is within the top 20.

Johnson Enterprises, I think, is number 1, and they manufacture Soft-Sheen product, which is the same.

Chairman WYDEN. So it is your view that this product is widely distributed.

Mr. KARP. Absolutely; thousands, probably millions of women have it.

Chairman WYDEN. Now you said as a result of the litigation that you were involved with Ms. Green you received calls from around the country.

What were these calls about? What kinds of cases where people bring to your attention?

Mr. KARP. You should first know the company said this, you know, was a fluke, and that it was just a coincidence that their product was on the hair when the hair caught on fire.

Then I started hearing from lawyers with amazingly similar incidents. Not only were women lighting matches and catching their hair on fire, I had a call from somebody whose client walked by a barbecue, and the spark from the barbecue came on and caught her hair on fire.

They were all over the country. We had calls from Chicago, New York, Philadelphia. The identical incidents were occurring with young black women who had used this or a similar product.

We knew after I got all those calls that obviously you cannot have the same coincidence happen in different sections of the country in the same way.

Chairman WYDEN. Could you give us for the record a summary of those cases that are based on information that you got from around the country?

Mr. KARP. I could provide to your subcommittee the names of the lawyers who contacted me so that they could be contacted.

Chairman WYDEN. That would be very helpful.

Is your client presently employed now?

Mr. KARP. No; she is not employed.

Chairman WYDEN. Is she just not able to work?

Mr. KARP. She had been on welfare when this had happened, and the chances of ever being employed now are remote because she cannot go out in the sun.

Chairman WYDEN. Now you mentioned that the company that made this product said that the injury was a fluke and that there really was not any relationship between the hair fire and the product. What did you say to the company when they said that?

Mr. **Karp**. We asked them for prior incidents. They said it was irrelevant as to prior incidents. They refused to produce them and we got the court to order them to produce prior incidents.

We had those. We knew obviously it was not a fluke. They had been told before.

Chairman **Wyden**. Their defense is that hair burns. It is just a mere coincidence that it burns with this product on it. In fact, when the appeal was argued, one of the judges said to their lawyer, why do you even put the warning on here, "Keep hair away from open flame," if in fact you have such a safe product? They said our legal department told us it was a prudent thing to do because hair burns.

In fact, in the course of the trial, one of their defenses was, amazingly, if you put a hat on your head, a straw hat, and that gets ignited, it will ignite your hair. Should we start labelling hats?

Of course a hat can be removed, and a grease fire in your hair cannot.

Chairman **Wyden**. Have other legal actions been taken against this company for similar problems?

Mr. **Karp**. There have been several other lawsuits against this particular company. Some have been settled. I imagine some are still pending.

Chairman **Wyden**. You feel that this company and other firms are now producing products which are dangerous to people.

Mr. **Karp**. We had testimony at the trial that said that unless you give consumers a real warning—unless you let them know that they are walking around with a potential tragedy that can happen at any minute when they walk by a source of ignition, that the product—our experts testify the product ought to be taken off the market until you can either improve this problem, or until you can come up with a way to warn these people of the risks involved.

Chairman **Wyden**. Do you want something like a warning label that says keep hair away from open flames after using this product?

Mr. **Karp**. The problem with that warning is it leads people to believe that when you are putting the product on your hair you should not go near an open flame like a stove.

It does not let the consumer know that the next day, when all the water in this dries up and the residue is left on your hair, that it is far more dangerous the next day.

Of course a spark is not an open flame. It does not let women know what the real dangers are.

Our warning expert said there has to be a way of letting these people know that when you use this product for days afterwards do not go near any source of ignition.

Do not smoke. Do not go around anything that can catch your hair on fire.

Chairman **Wyden**. What happened when you contacted the FDA about this matter?

Mr. **Karp**. The FDA was extremely unhelpful, not because they did not try. They just said that this is really outside their bailiwick; they had no authority.

They suggested I contact the Consumer Protection Agency. We contacted them. We just found out that there is no real essential clearing house which requires these companies to label the product, which really tracks all of these complaints.

Chairman WYDEN. Now your firm got a judgment against this company.

Mr. KARP. Correct.

Chairman WYDEN. With respect to the action involving Ms. Green. As part of that judgment, was the company directed to make any changes, for example, to change its labelling?

Mr. KARP. The court really did not have any authority to order the company to make any changes. All the court could do was just uphold the verdict which is a money judgment.

I think the only way you can get them to change the labelling, unless they do it themselves after the cases similar to mine, is to pass some sort of legislation which would require them to submit the label maybe to the FDA beforehand to make sure that it adequately informed consumers.

Chairman WYDEN. Are there other legislative or administrative changes that you think are necessary to protect the public as a result of your experience?

Mr. KARP. It seems to me that especially as a result of what I heard this morning there ought to be some essential clearing house.

There ought to be a committee, if you will at the FDA where any product that you are going to put on your hair has to be submitted to them with all the risks.

Then you have to submit, seems to me, some sort of a label. I bought a product for my son—my infant son the other day, and I noticed the label which now appears in every plastic bag in this country, says, "Plastic bags can be dangerous. To avoid danger of suffocation, keep this bag away from children."

Well, there was a time when babies all over the country were getting suffocated because of picking up plastic bags. You cannot buy a product in this country now that has a plastic bag that does not have a label like this on it.

It has, I am sure, saved countless lives of infants, and it only costs a penny or two to put something like this on every plastic bag. They ought to be doing this to cosmetic products.

Chairman WYDEN. Why do you think manufacturers are not putting this kind of labelling or other information on it? It would seem to me that in one sense it would be a sound business decision because certainly, if there are problems, there is a statement there, or a warning, or a label, or something to that nature.

Now maybe the flip side of it is that if you give people that information they sell you a product.

Mr. KARP. I think there are fears—I think it is a public relations fear. I think there are fears. If they really let women know what can happen to their hair they are not going to use the product, or they are going to buy a different product, which is the whole idea, to give the consumer a choice.

Chairman WYDEN. You have been very helpful, Mr. Karp. We thank you.

Mr. KARP. Thank you, Mr. Chairman.

Chairman WYDEN. We will look forward to working with you as well.

Dr. Cone, you went through four cases which struck me as severe cases of occupational exposure to a variety of cosmetics.

Is it your view that these are not isolated cases, but happen fairly regularly?

Mr. Cone. Not only are they not isolated, but really unfortunately, we see only a few of the many that are going into emergency rooms, seeing the multiple physicians, talking to their cosmetologists, or talking to their employers, and never get out beyond that.

I think only a few of what we suspect are a much, much larger group.

Chairman Wyden. What about the work environments that you have described, the working conditions and the chemicals? Again, is this a fairly common kind of occurrence, or one of a more isolated nature?

Mr. Cone. The descriptions that you heard today from the two victims were really, unfortunately, typical of this industry—that it is largely in relatively smaller shops, which may not have the most up-to-date ventilation equipment for many reasons, one being cost.

But also, there is, I think, a lack of information that may contribute to this lack of adequate ventilation. That is, I think, unfortunately typical of most places that I have actually visited that really are almost industrial settings, where they are mixing plastics, making chemical solutions without the benefit of proper ventilation.

In this industry, normal industry, you would have local ventilation right there at the spot, taking away the fumes. It is just not common practice in the cosmetology industry at this time.

Chairman Wyden. Now you have a lot of experience working with patients. On the basis of that, do you think that there are a significant number of cosmetic products which, if used by perfectly healthy people would subject them to short- and long-term health effects?

Mr. Cone. I am not particularly consulted by consumers. So I cannot comment, except that most people in this country use one form of cosmetic or another.

So I cannot comment on how widespread this problem is in the consumer area.

However, we do hear from the cosmetologists that we work with that their clients also have some of these problems.

I have clients who have asthma, or who have sensitivity of one sort or another to the skin, to their eyes, who can no longer go to the salon; no longer can even consult them because of their reactions to these products.

Chairman Wyden. But people who have these adverse effects, these short- and long-term adverse health effects, these are people who, based on your experience, would otherwise be healthy?

Mr. Cone. These are your average people. These are not specially sensitive, necessarily. They are unfortunately people who maybe encountered the products at a higher concentration than average maybe, or for longer periods of time, which may then provoke a response.

But it is the kind of response that given enough time or enough amounts would affect almost anybody if a sufficient concentration was present.

Chairman WYDEN. Have there been adequate epidemiological studies to really look at the actual long-term health effects in humans of these products?

Mr. CONE. I would say no. In fact, there are a few studies. I have cited a few representative studies in the end of my testimony. But I brought them here. They are studies that demonstrate occupational asthma in a beauty salon. One study looked at 20 workers and found that 4 of them, in fact, had occupational asthma. This is one small salon. They found 4 workers very similar to the case we heard this morning.

Chairman WYDEN. Without objection we will put those studies into the record. That is very helpful.

Mr. CONE. Fine; there are a number of studies—actually the most prevalent problem is the problem of skin problems. Contact dermatitis it is called, which is a result of either irritation or allergic reaction to many of the products used in the nail products or in the perms, or various shampoos, and some of these particular substances are very well identified. There is enough information to know which ones are the worst in terms of producing those reactions on the basis of several of these studies.

There are several investigations of cancer, and I think that is certainly worrisome—one published by the Journal of the National Cancer Institute.

This reported a study of a group of over 10,000 cosmetologists in the State of Connecticut and found an increase in the rate of cancer overall in this group.

That is very worrisome. I think it needs to be taken into account when we look at the product label and see some potential carcinogens present.

Chairman WYDEN. But I do want to come back to this question cause I think it is a key one.

Have there been, in your view, adequate epidemiological studies so that we could look at the long-term health effects on humans?

Mr. CONE. No; in most of the products, no. I would say that.

Chairman WYDEN. The only other question I think I had for you at this time is has the absence of ingredient information on hair care and nail care products used in beauty salons in schools hampered the ability—your ability and that of other physicians—to effectively treat patients?

Mr. CONE. I think that is an excellent point.

Yes; we have had difficulty, as I have mentioned, in identifying what products, or which compound, or which chemical—even the name of the product is sometimes difficult to find because of the use of unlabeled bottles.

We are just being forced to tell cosmetologists, I'm sorry, we cannot really tell you which product or which chemical—we are going to have to recommend you to leave this industry.

It is a major economic and social cost that is being born by the individual cosmetologist.

Chairman WYDEN. The only other question I had, we heard from Ms. Shulman with respect to these occupational safety and health standards, OSHA standards, with respect to hazard communication, and her view that they did not seem adequate to deal with the issues that we are talking about. Would you agree with that?

Mr. CONE. I think that hazard communication is, in my experience, a necessary ingredient, but material safety data sheets alone are not sufficient, and often, even if they are present there is not adequate amount of chemical labelling in the material safety data sheet. It is either inaccurate or insufficient—in other words, there are ingredients that are not even listed—or it is not available; it simply does not make it through the chain of distribution.

So the material safety data sheet is very helpful, but it is often too late to warn the worker. It may be available only after we have figured out that this particular product is a suspicious product.

It should be available, and readily available in any salon. However, a label on the product itself will make a much better warning to the actual person using the product.

Chairman WYDEN. How do these work places that we are talking about compare from the standpoint of dangerousness to manufacturing plants?

Mr. CONE. I think that is a difficult generalization. But I think in general manufacturing plants, particularly chemical manufacturing plants, are very conscious of potential hazards of their ingredients, the processes, and of potential leaks, for example, which may actually cause the problem.

Therefore, they tend to use closed processes. They are usually, in my experience, much more conscious about the potential for respiratory and dermatologic problems to the point that they protect people because they have had the experience in the past of adverse reaction.

Chairman WYDEN. But they may well be the same chemicals.

Mr. CONE. They are often the same chemicals. But I think the fact that they have enclosed the process, they provide respiratory protection, skin protection, indicates they recognize there is a problem. I think the problem here is lack of recognition.

Chairman WYDEN. I want to thank you. You have been very, very helpful and very patient. We will be in touch with you, I know, in the days ahead, and unless you have anything further to add we will excuse you at this time.

Mr. CONE. Thank you very much.

Chairman WYDEN. Thank you both.

Dr. Gary Grove, Ph.D., vice president, KGL, Inc., Ivy Laboratories, Springfield, PA.

Dr. Grove, we are going to get a name tag for you. But before we swear you in, I just want to express the subcommittee's appreciation for your being here.

I know that you are here at a time of great inconvenience to you personally at a time when certainly from a business standpoint you had a full agenda there at home at Springfield, PA.

I just want to thank you personally for your courtesy and for coming because it is very gracious of you. I appreciate the chance to talk with you the other day as well.

We are going to start and just set that clear right at the outset. Now Dr. Grove, it is the practice of our subcommittee to swear all the witnesses.

Do you have any objection to being sworn?

Mr. GROVE. Certainly not.

[Witness sworn.]

Chairman **Wyden**. Dr. Grove, we will make your prepared remarks a part of our hearing record in their entirety. And if you could in your oral presentation focus on your principal concerns it would be very helpful.

Mr. **Grove**. OK, thank you.

## TESTIMONY OF GARY GROVE, Ph.D., VICE PRESIDENT, KGL INC./ IVY LABORATORIES, SPRINGFIELD, PA

Mr. **Grove**. I am very pleased to participate in these hearings. Hopefully, I will be able to provide some insights that will allow your subcommittee to be more informed of the important issues that you are concerned with.

I have been actively involved in skin care product development and claim substantiation research for approximately 15 years.

Currently, I am the vice president of research and development of KGL, Inc., and head of their skin study center outside of Philadelphia.

This is a privately owned independent testing center that I am very proud to say has earned an international reputation for its innovative work in monitoring changes in skin structure that function noninvasively.

We evaluation the safety and efficacy of topically applied products. Our clientele is broad based and represents all aspects of the cosmetic industry, includes both cosmetic companies and pharmaceutical firms.

We work strictly on a fee for service basis, and as such do not endorse products, or receive royalties from their sales.

What is important to us is that we adequately judge whether a product is safe for its intended use, and can perform as well as its manufacturer claims.

Now it is quite clear that the veracity and integrity of the skin care product industry is being brought into question by a number of groups.

If anyone were to ask me 5 or 6 years ago how much science is there behind the ads being made, I would have been the first to admit that there is a lot more science fiction than real science.

However, this is clearly no longer the case. In fact, the truly innovative research programs that are being conducted to study various aspects of normal skin, physiology, and cutaneous aging are more likely being funded by these commercial interests.

While there is no doubt that some truly outlandish claims are being made, for the most part these are the handiwork of here today, gone tomorrow companies.

I feel that most of the established companies are going to great lengths to ensure that their products do indeed live up to their claims.

Now this is not to say that their advertisements are based solely on fact and contain no fiction. Some degree of puffery has always been tolerated, and inadvertent misrepresentations of data do occur.

However, it is unlikely that any reputable firm has intentionally lied in their advertising for the very simple reason that we now do have the capabilities to either confirm or deny these types of claims.

Now it should be appreciated that the skin is highly complex in its function, composition, and structure. Nevertheless, it has certain cosmetic defects, such as being too dry, too rough, too greasy, too aged, et cetera, that can be recognized quite easily.

By clearly defining these defects, we can create the necessary basis for developing scientific methods by which the degree of success of skin care products designed to alleviate these conditions can be measured.

In actual practice this might not be as straight forward and easy to do as one would wish. But such an approach has become an important part of successful product development, and critical in creating competitive marketing strategies.

There is considerable consumer interest in products that deliver readily perceivable benefits that are the result of these scientific advances.

Nevertheless, we must always appreciate that consumers are highly susceptible to advertisements that claim product, especially if endorsed by celebrities, even if they have no credentials in the cosmetic or skin care science.

Otherwise, reasonable adults can easily be misled into purchasing various products, devices, and treatments that could not possibly live up to their claims of providing rejuvenation and eternal youthfulness.

It is true that if false or greatly exaggerated claims are being made for a product the user will soon discover that it does not perform as promised, and thus will not buy it again.

This may be of no consequence to a company if their marketing group is interested in a successful launch instead of a successful product.

However, over the long-run such a strategy could be proved disastrous. Indeed, the failure of a product to live up to a static claim can have a ripple effect that makes potential customers skeptical of other offerings in that mind, if not the overall brand.

The recent introduction of a new class of antiaging products that promises to retard or reverse the signs of aging has prompted the FDA to serve notice that many of these treatment claims fall under the drug definition of the law.

Determining how far one may go before a performance claim will be deemed a therapeutic claim that subjects the product to regulation as a drug is certainly a critical issue.

Whether the more than 50-year-old Food, Drug and Cosmetic Act needs to be revised to reflect the recent technological advances made in the cosmetic and skin care science should be carefully considered.

Obviously, if the manufacturer can formulate and distribute a cosmetic drug product in accordance with an FDA monograph, such as a skin protective, acne or sun screen monograph, I think they would be well advised to do so.

It is important to note that in this recent flurry of FDA activity, the safety of these products is not an issue. This is not surprising since most cosmetic companies do considerable premarket testing to establish the safety of their newly created products.

Indeed, the industry should be praised for the approaches taken to self-regulation since it worked so well.

The key ingredient to the success story is the CTFA, the Cosmetic Toiletries and Fragrances Association. This large group of manufacturers strongly urges that all companies actively participate in the voluntary reporting program being conducted by the FDA.

The CTFA also has published technical guidelines that cover the general concepts of what is entailed in adequately testing a product for safety.

The CTFA has also been interested in organizing the CIR, the cosmetic ingredient review. This consists of an independent panel of expert, toxicologist, dermatologists, formulators, and so forth, who are systematically and thoroughly evaluating cosmetic ingredients from a safety point of view.

As you might well imagine, this is an enormous undertaking. Priorities based on the degree of use has been established, and considerable progress has been made in going through the list, with the information being gathered shared with all interested parties.

Now this does not mean that there is not some room for improvement. For one thing, the FDA is severely limited in both manpower and funding, and if it is to remain an effective watch dog, this must be remedied.

I also feel that the potential for a safety problem to emerge is considerably greater with small businesses, as they most likely do not have the resources to do adequately in-house safety testing.

I am especially concerned that some beauty shop operators, cosmetologists, and estheticians, are becoming more adventuresome in creating home-brewed remedies for their local patrons.

Now how they can be properly regulated without adversely affecting their businesses is not, at least to me, readily apparent.

It is certain that various consumer groups and regulatory agencies will continue to impose greater responsibilities on the manufacturers of cosmetics and skin care products to ensure the safety and efficacy of newly marketed formulation.

In light of this trend I would like to strongly urge the manufacturers to make a voluntary effort to develop guidelines if they find unacceptable marketing and promotional practices, as well as standardizing the method and analytical techniques used to generate these performance claims.

These principles of conduct guidelines should specifically advocate advertising claims that stress product performance claims that can be scientifically verified.

They should also stress that all instrumental tests be relevant to the real world, and always be supported by appropriately designed, subjective assessments by nonbiased panelists and expert graders.

Clearly, these guidelines must not condone advertisements that make unsubstantiated assertions. They are designed to impress, bewilder, and/or alarm the consumer.

With that I would like to make myself available for any questions that you might have on these or related matters.

[Mr. Grove's statement may be found in the appendix.]

Chairman Wyden. What percentage of companies are represented by that organization, the CTFA?

Mr. GROVE. I really do not know. I think that would be a more appropriate question to ask the CTFA. I am under the impression that most if not all of the large companies are members.

It also includes many small businesses as well. But I really do not know the actual breakdown of their membership. But it is the industry trade association.

Chairman WYDEN. With respect to testing for health effects, do you think that adequate testing is now being done for long term health effects?

Mr. GROVE. No; because no one is really addressing the long-term health effects. In our skin study center, most of the tests are short-term, toxicology, allergic responses and so on in which the panels are exposed to the products for 1 day, 2 days, 1 week, and so on. There are really no long-term studies going on.

Those would be impractical to do. What I think that the industry is doing is largely relying on epidemiological data and literature references, and so on, to look at those long-term effects.

Chairman WYDEN. Do you think it is impractical to do long-term studies?

Mr. GROVE. I think it really depends upon what your definition of long-term is. I have done a lot of work in aging. It is very difficult to look at long-term effects because some things change very, very slowly.

We can talk in terms of years and so on. It is very difficult to envision an experiment where you place individuals on particular ingredients, expose them, et cetera, et cetera, and look at the consequence of that exposure at 6 months, 1 year, 2 years. How long is long-term?

Chairman WYDEN. Do companies set up control groups, for example, to test their products over a 5-year period or something of that nature?

Mr. GROVE. Not that I am aware of.

Chairman WYDEN. Do you think something like that ought to be done?

Mr. GROVE. Again, I am not sure how feasible that would be. I think the approach that they are taking is a much more rational approach.

Essentially that is what the CIR does is, they have created a list of ingredients that are based on their use, and are systematically and thoroughly going through that list.

They are asking the various companies that have experience with those ingredients to share with them their safety data. They are also doing literature searches to see whether or not—in the scientific literature or the public press—there is not any evidence of their being problems with these particular ingredients. And so they are doing it that way.

Again, it would be a very interesting thing to do, but what ingredient would you like us to test over a long period of time? There are so many. And there is just so much time and money you can commit to these types of long-term studies.

Chairman WYDEN. Let me make sure I get the facts with respect to how many cosmetic ingredients have been examined by the CIR. Now it is my understanding, according to a press response to the hearing, that 300 of the commonly used cosmetic ingredients have been examined by CIR. Aren't there something like 8,000?

Mr. GROVE. If you start off with what is in the CTFA dictionary, which I think is probably a good place to start, there are approximately 4,000 ingredients in the CTFA dictionary. These are the things the suppliers are offering for sale. If you go through essentially what is happening, you must also be aware that there are other groups that are reviewing some of these ingredients, such as the color additives.

There is the RIFM, the monographs of the OTC reviews and so on. It boils down to the fact I think that they've recently come up with a list—actually it contains 458 that have not otherwise been considered, and are being evaluated by the CIR.

These are essentially the hit list, and they are essentially looking at those that are most widely used. There is something like 700 that are actually used in 20 or more formulations in the last 2 or 3 years, and of those, most of them are being reviewed by other agencies, and there is a remaining 458.

Of these, as you already have alluded to, approximately 300 have been completed—actually, 288, and there is 54 currently being processed. There is 116 being scheduled.

I think it is important to note that of the 288 that have been so far reported on, most of them have been classified as being safe as used.

There have been some problem products. Those problems have largely been in terms of concentrations in the formulation—or the form that those products have been used in.

There has only been one that has been deemed unsafe, and that particular product, or that ingredient was removed from the marketplace before the review process was completed.

So this is what I mean when I say that I think the CTFA and the CIR are really doing a very good job. I really cannot think of any other way to approach the problem, given the enormousness of the problem.

Although I am a scientist, and like to do carefully controlled experiments and so on, I just cannot fathom how I would systematically go through all the myriad of ingredients that are available for the cosmetic formulator to use.

Scientifically, under carefully controlled conditions, whether they be animal studies or human studies, eliminate them from consideration.

Chairman WYDEN. With respect to testing—and you get many products, and are in a position to in effect evaluate the claims that people are making.

Of products that you have tested, do a significant number of them not live up to the product claims that are being made?

Mr. GROVE. If we are talking now about performance claims as opposed to safety testing, I would say that yes, they do. But if you talk in terms—

Chairman WYDEN. Let's get both of them. I would like to know on both product claims and safety claims whether a significant number of the products do not live up to the claims.

Mr. GROVE. OK, in the safety claim issue, essentially the decision would be there whether to market the product or not, and to the best of my knowledge, any product that we have ever seen have a safety problem associated with it has never been marketed.

I think our clients are very, very concerned. The last thing that they want to do is market a product that comes back to haunt them because there have been numerous customer complaints of their being adverse reactions, and so on.

This is particularly important to large companies that have a brand name that they want to maintain a good reputation. But it would be a disaster if one of their products would have a bad press associated with causing problems, and so on.

But there is a problem. The problem is that we also have within the cosmetic industry roughly three types of companies. We should perhaps talk about them because how I feel about certain aspects changes, depending upon what type of company we are talking about.

First of all, we have the here today, gone tomorrow—the fly-by-night companies.

Chairman WYDEN. How many of them are there?

Mr. GROVE. I do not know.

Chairman WYDEN. Is it thousands?

Mr. GROVE. I really have no idea because they do not have to register with anyone. You can essentially go to the Sunday supplement advertisements page, and you will see ads that make outlandish claims for not just cosmetics—weight loss, hair restoring, and so on.

So there is a whole industry there. One of the more recent ploys is to rent time on TV and have sort of documentaries, and again have an 800 number that you can phone in with your credit card and order the miracle product.

Chairman WYDEN. But it is your view that there are a significant number of these fly-by-night companies making outlandish claims?

Mr. GROVE. Right; I am more concerned about them than I am with the major manufacturer. I am not so concerned about whether or not there are any safety issues because invariably what these guys are doing are making very ineffective products made out of very bland ingredients. Their major goal is to create money for them, and they are not really doing anything adventuresome in terms of——

Chairman WYDEN. Who is doing that, the smalls or the bigs?

Mr. GROVE. The smalls. I mean we are talking about independent entrepreneurs here.

The small companies, I think, are generally concerned in trying to produce quality products. The problem with the very small companies, of course, is that they have limited resources, and may not be in a position to do adequate testing.

Of course, then you can range from there on in, up to the larger companies—I think when you start talking about the larger companies they also are honestly attempting to provide quality products.

Here, they obviously do have adequate facilities to do the testing. I think that they are doing that testing, and I think they are doing over and above that which is required by law.

The reason that they are doing that is because they want to maintain a very good reputation for their brand names.

I think you should also be aware—and I was very happy to hear that you say you are an advocate of voluntary testing procedures because if you start thinking about mandatory testing you must appreciate that it is going to have different impacts depending upon the size of these companies.

I do not think anything you will do will stop the fly-by-night companies. So they could care less about the law.

But many of your small businesses would be faced with increased cost, depending upon the extent of the tests that you had mandated for them to run.

The large businesses, I do not think would be affected at all. I think it would be status quo because they are already most likely running the test that you would mandate.

In fact if anything you could perhaps even be decreasing their costs because I suspect that whatever you would mandate might be below what many of them are already doing, in terms of testing for safety of their particular products.

Chairman WYDEN. Well, let's go to some of these claims for these major companies, then, if we could for a moment. Put them up on the chart. But I am going to read you a few.

Mr. GROVE. OK.

Chairman WYDEN. Channel Lift Serum Anti-Wrinkle Complex, 45 percent wrinkle reduction, clinically proven.

How would we know that that was a truthful claim?

Mr. GROVE. OK, first of all, let me disavow my involvement with any of the products that you have selected to illustrate today.

Chairman WYDEN. I know.

Mr. GROVE. We can talk about that one.

Chairman WYDEN. I understood that. And I only want to ask you about it because you had——

Mr. GROVE. OK.

Chairman WYDEN [continuing]. Talked at some lengths about large companies. We have collected some of these claims. How would we know in the case of Channel Lift Serum Anti-Wrinkle Complex that there was evidence showing 45 percent wrinkle reduction?

Mr. GROVE. OK, if someone were to come to me and ask for me to substantiate that type of claim, I would use a technique called image analysis——

Chairman WYDEN. No, no, I understand that you would do that because we know of your expertise.

Mr. GROVE. OK.

Chairman WYDEN. But how does the public know?

Mr. GROVE. Unfortunately, they do not. That is essentially what I am trying to establish, is that there will be—and again, I would like to have this done on a voluntary basis that the manufacturers would agree among themselves that if you are going to make this type of claim that this would be the appropriate technology to use to support that type of claim so that the numbers start meaning something to people.

I think probably the best example of what Uncle Sam has done for the U.S. consumer in terms of the cosmetic and drug industry is the SPF number, the sun protection factor, because the consumer can look at those numbers and determine, first of all, that a factor of 15 is better than a factor of 8; it is better than a factor of 4, and depending upon their particular sun sensitivity, it might be more appropriate for them to use one factor or the other.

That is completely lacking in terms of evaluating other types of these claims. What I am suggesting is that there could be some basis of comparison for the consumer that indeed we adopt standard performance tests that would allow, much in the same way that we have SPF's that we could have other types of readily recognizable yardsticks by which product performance can be measured.

Chairman WYDEN. That sounds like an interesting suggestion. And one will certainly want to follow up. But let's go through the rest of these.

Estee Lauder night repair cellular recovery complex enhances the natural rate of repair or cell damage by the ultraviolet light. Laboratory tests show a 37- to 38-percent rate of increase in the natural repair of cell damage.

Now again, as of now, the American consumer cannot get any proof with respect to that claim, can they?

Mr. GROVE. No; obviously—again, I was not involved with that particular product. But I would assume that Estee Lauder has in their files documentation, laboratory reports, and so on that would allow them to justify that claim.

I think the issue that you may want to talk about more so than what you are doing is you have there labeled cosmetic product claims. I would take issue with that because I think what you have there is a drug product claim.

We really need to address that issue.

Chairman WYDEN. Do you want these products regulated like drugs?

Mr. GROVE. OK, I think we should talk, first of all cause you are often bewildered when we talk about the drug/cosmetic labeling issue. What bewilders people is that they find it hard to believe that what determines whether a product is a drug or cosmetic is not what is inside the bottle, but rather the claims that you were making for those ingredients on your packaging label.

I loved your scenario earlier this morning. You were talking about going home with your son and creating a cosmetic company.

In fact, instead of rushing back to Philadelphia, I would like to join the two of you in that endeavor. I think we might have a debate at whether we should call the product Gary's Goop or Wyden's Wonder Cream. But we could be in business this afternoon.

What we could do is if somehow we could find some Retin-A we could stick it into the bottle and package it in a nice pleasant way and so on. The claim that we would like to make so that it would only be a cosmetic product would be—let's make just a typical cosmetic claim that means "will help you regain that lost appearance of youthfulness."

Now I do not think we have time or even need to go through the FDA definition of what constitutes a drug versus a cosmetic on an individual word basis.

Cosmetics roughly are products that are designed to enhance personal appearance. All the beauty aids, lipsticks, rouges, eye shadow, mascara foundations, and so on are beauty aids and of course would fall under the cosmetic category.

If you took the position that eye shadow, mascara foundations, and so on are beauty aids then of course it would fall under the cosmetic category.

If you took the position that dry skin looks rough and scaly, and very unattractive, and if you use a moisturizer which would relieve the signs and symptoms of dry skin, and thus make the individual much more attractive, then, under that approach, also a moisturizer would be considered to be a cosmetic.

If we talked about using makeup in such a way that we could camouflage the wrinkles, hide them, that type of action also would be a cosmetic action, if we somehow camouflaged the wrinkles under make-up.

On the other hand, if we start dealing with drugs, the definition of a drug is—there is two aspects to it. It is products that are designed to be helpful in diagnosing, treating, or preventing disease.

Here we have a problem. Obviously, if we are talking about psoriasis or pityriasis, or any of a number of really frank dermatological dysfunctions and disorders, there is no question if you use any product that does anything to those types of disease entities that they clearly are drugs.

But as dry skin, the common everyday garden variety of dry skin, is that a skin disease or not? If you take the position that is a skin disease then we have a drug—moisturizers are a drug. So we have a problem there.

Chairman **Wyden**. But those are those antiaging creams.

Mr. **Grove**. No; I am just talking now in rough terms because what happens, with the FDA—the current definition of a drug, depending upon how strict you are in interpreting that definition, everything is a drug because the second aspect of the definition is that anything that alters skin structure function, actually the law says body structure function.

But here we are talking about skin—anything that alters skin structure function is a drug. I can tell you with our techniques that we have available at the skin study center, we can prove that just spritzing water on the skin surface will alter its structuring function.

Its electrical properties will be changed. It will be made softer, more compliant. The penetration of certain agents, noxious substances and so on will be enhanced or diminished, depending upon the hydration state and so on.

So if you go under that strict definition, then everything is a drug. But we don't have to worry about that in our little business because we are not making any type of claim other than our product will help restore that lost appearance or youthfulness.

Chairman **Wyden**. That is certainly under today's arrangement. We can make claims and go to work. But the claims up there, based on my knowledge at this point, seem to alter skin structure.

Mr. **Grove**. Absolutely; the FDA has—I'm not sure with regard to the specific products, but I suspect that every one of those has received a regulatory letter from the FDA on that exact issue.

Most of those manufacturers, I think, have complied with the law in some way or another. I think what might be surprising when people have trouble understanding is how they have complied with the FDA regulatory action.

Chairman WYDEN. Do they contain ingredients similar to Retin-A?

Mr. GROVE. Some of them do. Some of them do have retinal esters. if we again go back to CIR review data you will find that indeed a couple of months ago the CIR has reviewed retinal palmitate which is, again, because it has already been completely reviewed, an indication that the ingredient is being fairly widely used in a wide variety of products, not necessarily just the antiaging creams, and has been viewed as being a typical, safe, cosmetic ingredient.

Again, going back to the law, what the law is based on is not on what is contained within the bottle, but rather what the manufacturer is claiming those ingredients do.

That is the problem that you have. Because in our scenario, where we created our own company, I am putting Retin-A in that bottle. I am saying that we can manufacture that and sell it as a cosmetic.

Chairman WYDEN. If they work as claimed, these things up there—for example, the next one I was going to ask you is about this F29 complete antiaging complex. "Wrinkles will be measurably smoother and skin will be visibly younger-looking within 21 days."

If that product works as claimed, should it be classified as a cosmetic or as a drug?

Mr. GROVE. If they make that claim it has to be classified as a drug. But if the manufacturer chooses not to make that claim, it can be sold as a cosmetic under the existing law.

In fact, our scenario is even more—it is obvious that we could support any claim that we want because in our product we actually have an agent, an ingredient that is known to be a very effective antiaging ingredient.

Now the situation is——

Chairman WYDEN. Give me a second. These products that make the change in the skin, what do they contain in——

Mr. GROVE. As I mentioned, just water itself can make a change in the skin.

Chairman WYDEN. What about——

Mr. GROVE. It is hard to believe but if you interpret the law, or the definition in its strictest sense, anything that has older skin structure and function. There is a big difference between the skin that is here, and the skin that is covered by this shirt because the hydration states are different, and all sorts of properties of skin are dependent upon hydration properties.

Chairman WYDEN. What about Retin-A?

Mr. GROVE. Retin-A in what? In the situation I am saying, obviously the FDA would not allow us to go too far in marketing that product.

But the approach that they would take against us is not labelled as a drug or cosmetic. What we would say, of course, we are going to do it as a cosmetic. That forces us to put the ingredient labeling on the package. Now we could be bad guys and not mention that there is Retin-A in there. If we did that, of course we are guilty of mislabeling, or misbranding.

If we did put that there is Retin-A in the product, then I am sure that our friends at FDA would look at that. They will come as far as the safety issue is concerned because they would take the position—and this is the right position—that by having Retin-A in that bottle, we are essentially advocating the individual use of it without supervision or the advise of a physician as a prescription item.

I do not think we could stand up in a court of law at all, and try to support indeed that we have a cosmetic product that should not be regulated as a drug.

But it is not on the definition of what constitutes a drug or cosmetic that they are coming after us. It is because of the safety issue.

I think that is what is important. There have been some comments made today that under the law no one really has to do testing.

That is not quite true because if you do not have knowledge that your product has been adequately tested, I am led to believe—I have never seen it—but I am led to believe that the law requires that you put a warning statement, which is essentially called the black box statement that says that this product has not been adequately tested for human use.

Now I have never seen that on a product because I think if you try to market it—if we marketed Gary's Goop or Wyden's Wonder Cream, and admitted that we have not really done the safety testing and were willing to go that route, I do not think we would sell one jar.

So I think that it is a little bit of a misstatement that there indeed is a requirement. Now what is not clear is what constitutes adequate safety testing.

As I mentioned before, I think that there are some concerns, particularly among very small manufacturers, that they may not have the resources to do it, and so on.

But I am not concerned about major manufacturers in terms of the safety issue. I am concerned that many of them may have crossed the boundaries of what constitutes a cosmetic claim, and they are now making claims in the therapeutic realm. But I am not really concerned about those products from a safety issue.

Chairman WYDEN. If those products over there, just taking those, worked as claimed——

Mr. GROVE. OK.

Chairman WYDEN. They are not regulated as a drug, how do we know they are safe?

Mr. GROVE. Again, it would be from scrutiny of what is in their ingredients, which would be listed on their packages.

Chairman WYDEN. But who would do that?

Mr. GROVE. That is a good question. I would assume that someone at FDA is reviewing them. I think one of the problems that we have is I do not think you really need to have any more regulations. But I do think you have to give the FDA the personnel and the funds for them to effectively enforce the regulations as they currently exist.

Chairman **Wyden**. As I looked at all those claims, you again are in an area where you cannot get the proof, and you have said that. They make these claims. You will have 45 percent wrinkle reduction and the like. You cannot get their proof.

But if you assume that they have worked as claimed, and they are not regulated as a drug, it is not clear to me how anyone is going to be able to assure their safety.

Mr. **Grove**. Now I really appreciate your concern. It is a very—like I said, it is a very bewildering issue in terms of what constitutes a drug and a cosmetic.

But I think that you would be well advised in one of your future sessions to have someone from the CIR, the Cosmetic Ingredient Review, to essentially go through the process because I think it is perhaps the best approach. It is the only way I can think of of really doing it.

It is systematically and thoroughly examining the ingredients. They have a hit list, and that hit list, I think, has been organized in a very appropriate way—that is, whatever is being used most widely is what they are looking at first.

They are more than halfway through the process right now. Again, I am very concerned about the entrepreneurs. They are very small businesses—these fly-by-night operations—because there is no regulations. But even if you create regulations, I doubt that they are really going to be compliant with them.

Chairman **Wyden**. I think you make a number of very good points. Certainly the question of smaller companies is a very serious one. I also want to be able to assure my constituents that those kinds of products are safe because those products are being sold widely—sold across this country.

Again, I operate under the assumption that you cannot get the proof of what they are saying.

Mr. **Grove**. The only product that I have been directly involved in is the Lancome Niosome Systeme. We did not evaluate that product for its antiaging properties, but rather for its moisturization properties in a group of senior citizens.

As part of that program we also looked at the safety of that particular product on a short-term usage basis. Here, short-term being a matter of 2 months. There was absolutely no problems with that particular product.

I really cannot talk about the other products because I am not actively involved with the research.

Chairman **Wyden**. I understand that. What I am interested in is if you err, as I think you always should, in giving people an opportunity to prove something and we cannot get the proof, you then operate under the assumption that it does work, the product is not regulated as drugs.

How can a legislator assure their constituents that it is safe. That is what we want to do.

Mr. **Grove**. But I think the only thing that we have going for us is that the major companies are very, very concerned about their reputations. If they have a problem with any products, that could have a very severe impact on their whole product line.

The fly-by-night operators are not concerned at all because you and I could create a cosmetic company today. We run into some problems; we will go up to Pennsylvania and create a new company with a new name. We have no problem doing so.

But the major manufacturers do have a problem because they are in business and they want to be in business today; they want to be in business tomorrow. They want to sell products. The only way they can sell products is, first of all, it has both to do with the safety and efficacy—they have to produce quality products that live up to those claims. If they have problems and individuals feel that they perhaps are not living up to their claims, they are not performing as promised, or if there is any predominant safety issues that causes irritation, hair loss, whatever, the word gets around. As soon as that word gets around, there is a big problem at that particular company, and they want to avoid that at all costs.

That is why I am saying that if you do mandate the legislation, I am of the opinion that many of the major manufacturers, if they would want to, could reduce their testing budgets, because I am sure that whatever you would mandate is going to be less than what they are already doing.

Chairman WYDEN. I am not sure that I agree with the view that the word gets around. Certainly, I do not think Ms. Greene would agree with it, whose lawyer we heard.

Mr. GROVE. That is a different area. My expertise is in the area of skin care products, not hair care products. I think that is a whole different story, in the beauty shop operations and so on.

I am also genuinely concerned about that. I think that is a whole different issue.

Chairman WYDEN. What about the labelling of these kinds of products? We heard concern about both the consumers and the representative of the USCW that there was a problem in terms of labelling and getting accurate information.

With respect to these products, are the ingredients understandably labelled on the product?

Mr. GROVE. You threw in an adjective there that is difficult to deal with. That is, understandably, because—and the previous witness, I think, made a very good point that you can have very strict labelling requirements, but if the terms are multisyllable, one, two, three, four, dyhydro—that means nothing to anyone.

So I think you have to be very careful about the labelling. Again, the CTFA dictionary is going to great lengths so that there are some common terms, and so on, so individuals can indeed identify these problem ingredients, and know what they are, and not necessarily use these very long bewildering chemical names. There is no question about that.

Chairman WYDEN. Are you satisfied that that information is now available?

Mr. GROVE. It is available in the package. Also, some companies—and I think particularly, one that I can highly tout for this is Mary Kay cosmetics goes to great lengths to make available to the physicians if they have a patient that has a problem with their particular product, they actually have a hotline number that they can phone in. At the annual dermatological meeting, the academy, they make available to the dermatologist formulation handbooks where they can, without calling in, look up—if they have Mary

Kay eye shadow 23, they can look up in the book and see exactly what types of things are in there.

Many, many more cosmetic companies are starting to interact, particularly with the dermatological group, either through the Derm Foundation or the American Academy of Dermatology, and are providing that information to the dermatologists.

Chairman **WYDEN**. You have been very helpful, Dr. Grove. We will want to talk with you as well in the days ahead. Thank you for coming.

The subcommittee is adjourned.

[Whereupon, at 1:46 p.m., the subcommittee was adjourned, subject to the call of the Chair.]

# POTENTIAL HEALTH HAZARDS OF COSMETIC PRODUCTS

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THURSDAY, SEPTEMBER 15, 1988

U.S. House of Representatives,
Subcommittee on Regulation
and Business Opportunities,
Committee on Small Business,
*Washington, DC.*

The subcommittee met, pursuant to notice, at 10:11 a.m., room 2359-A, Rayburn House Office Building, Washington, DC, Hon. Ron Wyden (chairman of the subcommittee) presiding.

Present: Chairman Wyden and Representative Price.

Chairman **Wyden**. The Subcommittee on Regulation and Business Opportunities will come to order.

Today, the subcommittee continues its examination of the health and safety issues that are increasingly at stake in the $17 billion U.S. cosmetics industry.

At our July 14 hearing, witnesses told us how dangerous these products can be. For example, the subcommittee heard from one consumer whose hair caught on fire after she used a hair spray and then lit a cigarette shortly afterwards. Now, she is permanently disfigured and in constant pain.

Also, at that hearing, cosmetologists explained how they had suffered irreparable nervous system damage, memory loss, and severe respiratory problems as a result of using cosmetic products.

The evidence that we assembled at that hearing indicates that consumers cannot be sure that the thousands of cosmetics presently on the market are safe.

The Food and Drug Administration, the agency responsible for overseeing the safety and efficacy of products, does not have the same broad-reaching authority to regulate cosmetics that it has for food and drugs.

After our first hearing, FDA spokesman Emil Corwin said that cosmetics should be subjected to the same standards as drugs and foods. He said, "We are the first to recognize that cosmetic regulations need to be developed."

Now, the industry contends that cosmetic ingredients are generally safe and innocuous. Since the subcommittee's first hearing on this issue, we have assembled information that would indicate otherwise.

The subcommittee asked the National Institute of Occupational Safety and Health to analyze 2,983 chemicals used in cosmetics. The Government compared these chemicals with their registry of toxic chemicals. This research indicates that 884 cosmetic ingredients have been reported to the Government as toxic substances.

Many of these 884 toxic ingredients produce or are suspected of producing harmful side effects, 314 are reported to cause biological mutation, 218 are reported to cause reproductive complications, 778 are capable of causing acute toxicity, 146 are reported to cause tumors, and 376 ingredients are reported to cause skin and eye irritation.

More alarming is the fact that of these 884 ingredients, only 56 have been reviewed or are being reviewed by the industry's Cosmetic Ingredient Review Board to determine their safety and related health effects when actually used in cosmetic products.

The industry's review board may discount these toxic ingredients due to the particular routes of exposure. The subcommittee believes that ignoring these reported harmful effects is a mistake.

In addition, since our first hearing, the subcommittee asked the FDA for a legal analysis of its current power to regulate cosmetics in our country. It is clear that these powers are extremely limited. The most the FDA can do to protect consumers is seize an occasional contaminated batch of products or ask manufacturers to change their advertising claims.

The FDA said in a letter to the subcommittee, dated August 19 of this year, "The agency strongly urges cosmetic marketers to conduct toxicological and other tests appropriate to substantiate the safety of their product."

But since the FDA cannot require that these tests be conducted, the FDA does not discover the harm a product causes until after a tragic event occurs.

Even the FDA's limited powers are rarely used. In fiscal year 1987, only 1 percent of the FDA inspections conducted occurred at cosmetic factories, warehouses or other establishments. The evidence further indicates that the limited powers that the Food and Drug Administration has are hard to exercise.

False or misleading labeling cannot be substantiated without proof, but the burden of proof is on the FDA and because they cannot legally require that testing data be given to them, misleading claims are not easily identifiable.

Second, the items listed as prohibited ingredients are almost exclusively unapproved color additives and do not include most toxic substances and even potential carcinogens, such as methylene chloride and formaldehyde.

While the industry does have a voluntary self-regulatory program, and it is a program that I think has a number of commendable features, it does not review all ingredients nor does it review all formulations.

It is my view that this program is no substitute for unbiased Government oversight. The industry's voluntary program does not even review all the ingredients used in cosmetics.

Although the Cosmetic Ingredient Review Board has reviewed nearly 300 of the most commonly-used cosmetic ingredients, indications are that many years will go by before nearly all of the thousands of ingredients are reviewed.

This could mean that as new ingredients are developed, the Cosmetic Ingredient Review Board will fall further and further behind in what is the only on-going and, I repeat, voluntary effort to investigate the safety of the products its members are actively marketing.

In addition, the subcommittee has been told by independent sources that the CIR may not be receptive to all concerned parties before deciding whether a particular ingredient is safe.

In essence, the industry's safety mechanism is a piecemeal patchwork system in dire need of repair. It is my view, having examined the evidence in the first hearing and accumulated additional information since then, that the industry essentially says to the American consumer: "Trust us, we know best, we'll make sure that safety issues are taken care of."

When proprietary matters are at stake, I think there are serious questions whether that is sufficient. At present, the Government cannot get information on specific ingredients and what is even more serious, it cannot get information on the possible interactions and formulations of the cosmetic chemicals.

So, we ask, what if the cosmetic ingredients produce a potentially harmful reaction, particularly as it relates to long-term effects. Our subcommittee is very concerned.

We heard testimony earlier that there was essentially no effort to look at the long-term health effects of these cosmetic products, and that is one of the most important health issues that we are going to address.

The fact is, as long as the data remains hidden in the pockets of the manufacturers, we are not going to know the full ingredients and the full effect of those ingredients on those who use them.

So, I believe today's hearing is a particularly important one. We intend to continue our inquiry into next year, particularly as the session is in its last weeks. But at today's session, we have the opportunity to get particularly helpful testimony.

[Mr. Wyden's statement may be found in the appendix.]

Chairman WYDEN. We are happy to have the Commissioner of the FDA, who, on all matters, has always cooperated with this Member of Congress. We want to welcome you, Dr. Young.

I think you know it is the practice of my subcommittee, as well as the other one chaired by Mr. Dingell, when we have occasion to visit, to swear all our witnesses.

Do you have any objection to being sworn?

Dr. YOUNG. Not at all.

Chairman WYDEN. Please rise and raise your right hand.

[Witnesses sworn.]

Chairman WYDEN. Dr. Young, we welcome you.

Let me also say thank you for the cooperation that you and your staff has afforded this subcommittee. They have been extremely helpful as we have tried to gather information on this subject.

We will make your prepared remarks a part of the record in their entirety, and why do you not make your oral presentation in a fashion that you consider appropriate?

## TESTIMONY OF DR. FRANK E. YOUNG, COMMISSIONER, FOOD AND DRUG ADMINISTRATION, PUBLIC HEALTH SERVICE, DEPARTMENT OF HEALTH AND HUMAN SERVICES; ACCOMPANIED BY TOM SCARLETT, GENERAL COUNSEL, FOOD AND DRUG ADMINISTRATION; AND RICHARD RONK, ACTING DIRECTOR, CENTER FOR FOOD SAFETY AND APPLIED NUTRITION, FOOD AND DRUG ADMINISTRATION

Dr. YOUNG. Thank you very much, Mr. Chairman.

I would like to introduce Mr. Tom Scarlett, General Counsel of the Food and Drug Administration, and Mr. Ronk, Acting Director of the Center for Food Safety and Applied Nutrition where the program in cosmetics resides.

I would like to highlight a few points in the prepared statement and then be fully responsive to your questions.

As you know, this is the 50th anniversary of the Federal Food, Drug, and Cosmetic Act that was passed in 1938. The common denominator, then as now, is that regulatory decisions be based on sound science, and this sound science needs to be updated continually.

In 1938, only a few ingredients we know today were formulated for cosmetics, and the industry had small numbers of manufacturers. Today, tens of thousands of cosmetics are distributed, and the number of ingredients has risen to an estimated 4,000 for producing a large number of different compounds.

The regulatory science has progressed as well. Originally, we were merely dealing with reactions on the skin. If you see it, test it. If it is positive by some sort of a patch test, avoid it.

We now are looking at more distinct reactions—toxic effects, such as immediate skin reaction, and contact allergy and systemic effects, particularly from inhalation and ingestion. I want to return to this point when we focus on what I think is one of the greatest concerns, the concerns for the cosmetologists who have to deal with these products in a very significant fashion in the workplace, where they are not labeled at all.

The number of ingredients has similarly multiplied, and we need to know, as you and others have pointed out, whether there are significant public health problems associated with cosmetic uses. If so, how do we deal with any that might exist?

The Federal Food, Drug, and Cosmetic Act, as amended, defines a cosmetic as an article intended to be rubbed, poured, sprinkled, sprayed, or introduced into the body or otherwise applied for cleansing, beautifying, and promoting attractiveness or for altering the appearance. Soaps are not included in the definition of the term cosmetic.

Specifically, in 1938, cosmetics were differentiated from the agency's authority in food and drugs, and later devices, because it was judged and has continued to be judged by Congress that though these products are important, they did not quite present the risk that the other products do.

Therefore, the act focuses on the issues that I have illustrated on that visual. First, the substances must be free of compounds that make them injurious to the users under normal conditions of use and, in that way, not be adulterated. They must be packaged in a safe and nondeceptive container; that is not misbranded or adulterated. They must be produced under sanitary conditions; in that sense, not be adulterated. They must be labeled with the information about the name and location of the product's manufacturer, packer, or distributor, and the weight or amount of the contents must be appropriately defined to avoid the misbranding charge.

Although the agency does not have the authority to review cosmetics before they are marketed, FDA does maintain surveillance of cosmetics and ingredients through postmarketing analysis. We have looked at only about 1 percent, but I am pleased to say, though the amount of our budget is small for cosmetics, I have increased it by 25 percent from 1984 to 1988. There are now 33 people who work fulltime in various aspects of our cosmetic program.

As we look at the term labeling and other written or printed materials, the label, as required by the Federal Food, Drug, and Cosmetic Act, must appear on the immediate product container as well as the outside wrapper.

The other act, the Fair Packaging and Labeling [FPL] Act, does not require immediate product containers to bear the ingredient labeling, and does not apply to the professional-use products that, through the gray market, may be extended to consumers.

This act merely requires and authorizes FDA to publish regulations which provide that consumer commodities, including cosmetics, must first bear the label statements of product identity, net quantity, and weight of contents. Second, they must bear label statements listing the ingredients, other than trade secrets, in order of descending prominence.

FDA is faced with an enormous task in meeting its responsibility to the American people. We have the responsibility for regulation of a $570 billion industry—25 percent of the consumer dollar.

We do this with a total cost per man, woman, and child in the United States of $2 per year. In the case of the cosmetic industry, the products are manufactured by 2,000 to 2,500 manufacturing establishments and distributed by about 4,000 to 5,000 firms.

We have a strategy that attempts to deal with this as expeditiously as possible. The first thing that we do is to evaluate consumer complaints of injury and adverse reaction. Second, we maintain cosmetic registries. Much of this in collaboration with industry. Third, we conduct some degree of scientific research on ingredients and develop methods for detection of adulterants.

Surveillance of the cosmetic industry and its products is an important aspect of our strategy.

Consumer education and industry education has been helpful, and I would like to submit for the record one of the publications of the FDA Consumer that focuses on that.

Chairman WYDEN. Without objection, we will put that in the record.

Dr. YOUNG. Thank you.

[The information referred to may be found in the appendix.]

Dr. YOUNG. We publish a number of regulations, one of which we are in the process of finalizing now. It is the regulation on the removal of methylene chloride from hair sprays.

We have felt this is something that needs to be addressed. We have some recent data that is in its final stage of evaluation, and we trust we will complete the agency's work by December of this year.

Chairman WYDEN. Excuse me for interrupting.

That is something that pleased the Chair of this subcommittee greatly because we had heard at our previous hearing that methylene chloride, which has been linked to cancers, is still being used in hair sprays. In fact, one of our former witnesses, purchased this bottle this morning here in the Washington area, and that particular ingredient, methylene chloride, has been linked to cancer.

The agency recommended that it be banned——

Dr. YOUNG. Unquestionably.

Chairman WYDEN [continuing]. In 1985, and, today, you are telling us that the agency has made a decision to actually go forward with the ban.

Dr. YOUNG. I want to say that a little bit more carefully.

The agency is finishing the evaluation of the last bit of data that has been submitted. Industry submitted some additional information. I spoke with Dr. Scheuplein this morning, and he has assured me that it is almost completed. The evidence that was additionally provided has not changed, to this point, the decision of the agency.

Earlier, we did put out the notice of proposed rule making. We anticipate completion of the agency's work within this year, if at all possible.

Chairman WYDEN. You expect to support the ban based on the evidence that you have accumulated?

Dr. YOUNG. Yes; I was pleased to sign the initial regulation, and I look forward to signing this one as well.

We feel that all the evidence indicates it is a hazardous substance. Just a mere introduction of this for a few seconds into the air in the bathroom every morning can produce some degree of risk, and I believe that it will be attended to.

I also have been pleased that since we announced this in the proposed rule, the number of manufacturers using methylene chloride has been decreasing. I was told that there has been about a 30- to 40-percent reduction already, even though there has not been a rule finalized in the marketplace. I think the marketplace knows the direction that the agency is going.

Chairman WYDEN. The marketplace did not know this morning when someone went and bought this.

Dr. YOUNG. I know that it is still on the market, but the proposed rule is out there, and that is a good signal.

Chairman WYDEN. We will have some questions. Please proceed with your testimony.

Dr. YOUNG. Fine; but I wanted to clarify that particular point.

There are a few areas that I would like to emphasize in the report I will be giving you in this testimony.

The first is that we feel adverse reaction evaluation in cosmetics does provide a sentinel indication of problems. For example, after the introduction of the new sun exposure product that contained a relatively large concentration of 6-methyl coumarine in the perfume compound, FDA received a number of complaints of irritation, swelling, and sunburn-like adverse reaction. Through investigations of the complaints and toxicological and clinical studies, it was identified that this ingredient was a cause of the reaction. The products in question and numerous other products were recalled, and the manufacturers voluntarily discontinued the use of this ingredient.

This gives us a chance to focus on problems, and, once the causal basis is identified, we can move rapidly. This is functionally how we meet those requirements.

Another area that I would like to call your attention to is the area of enforcement and regulatory actions. We try to be as evenhanded as we can, both in domestic and imported cosmetics. Over the period of time that I have been Commissioner, I have been particularly concerned about some of the compounds coming in from other countries. We have had some dyes that were banned in the United States, red 2, for example, that we recalled. We have had problems with labeling, where the labels were not in English, and we have had particular problems with eye shadows. So, we try to keep an evenhanded approach. We use wharf inspections and actual recalls and seizures as required.

We have dealt extensively with consumer education. One area that we feel particularly strong on is labeling regulations. I believe we have been able to issue labeling regulations under the authority of the Federal Food, Drug, and Cosmetic Act to approve warnings to consumers about safety problems. I would like to submit for the record the regulations that we have issued over the past decade and a half on that.

Chairman Wyden. Without objection, so ordered.

[The information referred to may be found in the appendix.]

Dr. Young. We also need to be aware of fraudulent claims that occur on a variety of compounds where new drugs are introduced into cosmetics. FDA has a vigorous program on two of these. One is in Retin-A. There has been a rush, unfortunately, to market Retin-A when the study merely consisted of 30 individuals in an experiment and 30 in a control group.

We have found that, in some instances, individuals were putting Retin-A into prepackaged creams illegally, mixing them in garages, and selling them to consumers.

Regretfully, individuals in the United States do not realize the potential dangers from using a medicine prematurely. In this case, the sponsor, Johnson and Johnson, is doing the right thing in looking to see whether there are any carcinogenic teratogenic effects. The black market is rushing extensively to try to influence our interests in the fountain of youth. Ladies and men, I have been told, are slathering this on their faces. Retin-A is a vitamin A derivative and, like the vitamin A derivative in Accutane, can produce birth defects. We feel that this is imprudent when we do not have the appropriate safety and effectiveness evidence.

The same has been true for Minoxidil, where this has been on the black market. In that case, the manufacturer, Upjohn, submitted a new drug application which recently has been approved for the use of this drug in baldness. There is a blurring at times between the line of cosmetics and drugs, and we intend to take vigorous action.

The final area that I would like to call to your attention is a problem about which I am particularly concerned and the agency is concerned: Labeling for professional use.

At the moment, cosmetologists are unable to understand the compounds they receive because the compounds are not labeled. I have been working and vigorously discussing this problem with the industry. I am pleased that they will be bringing forward a voluntary program today.

I have not had the time to study it, but I want you to know that I fully intend to see, that, if this program comes forward, it meets the needs that are required to help cosmetologists in their ability to know what they are working with, consumers to know what they are being exposed to, and the physician to be able to examine that further.

Chairman WYDEN. Dr. Young, let me interrupt for a second.

Dr. YOUNG. Yes.

Chairman WYDEN. It is your understanding that the industry will announce a new program in that area this morning?

Dr. YOUNG. Yes; it is my understanding they will be announcing it for the record. I have been working vigorously to point out this problem and I have been pleased that they have agreed. To the best of my knowledge, it is a multipronged program—one part dealing with providing information in the form of a label-type approach, another with education for the consumer, the cosmetologist, and others to follow through with manufacturers and State laws. I look forward to analyzing their testimony.

In a number of ways, there has been good collaboration and voluntary response on the part of industry. They have developed the Cosmetic Ingredient Review [CIR] to look at toxicological compounds that have been a problem. I know they have a number of educational approaches. In view of the law, we are focusing our efforts on strengthening this type of industry responsibility. I think it has been a good approach.

In summary, Mr. Chairman, I want to emphasize that the dominant concern of FDA as a public health agency is safety of the products we regulate for the consumers that use them.

There are cosmetic products with labeling which bears claims that the products are intended to change the cellular structure of the skin, thus claiming the users would be wrinkle-free and younger looking. With safety considerations at our forefront we have taken action against these products because they claim to have physiological effects on the body and cross over into the line of drugs.

In fact, if these physiological changes do occur from the use of the products, we must assure the public that these changes occur in a proper fashion. Manufacturers must demonstrate to FDA that their products are safe and effective for their intended use.

If any of the firms have data to demonstrate safe and effective use of their products, the data must be submitted to FDA for approval of the marketing claim for a drug before they market their product.

As a result of our actions, some firms marketing these products have relabeled and removed drug claims.

I believe you also know that we have submitted letters to a number of cosmetic firms, 23 in number, because they crossed that line. About 30 percent have modified those claims to date.

There are also legally marketed drugs for which the purposes would be considered cosmetic by many people who would look at these. These drugs, such as Minoxidil, which was recently approved by FDA to treat baldness, go through the new drug evaluation process, where the manufacturer demonstrates to FDA their safety and effectiveness.

Retin-A is also currently under review by the sponsor, and there are other examples as well.

As a physician, I also am concerned about the availability of information regarding hazardous ingredients in cosmetics used by cosmetologists in their workplace. These professionals, who use the products on a daily basis, over a long time, as well as the people on whom the product is used, should be able to ascertain what chemicals are in these products. I look forward to a solution to this.

The professionals and consumers exposed to these products as well as the physician who may be involved in a potential treatment, must be able to have sufficient information to be sure they can safeguard health.

I have recently been informed that the Occupational Safety and Health Administration has in place a comprehensive regulation on chemical hazards requiring manufacturers of cosmetics to evaluate the hazards of these products and transmit complete hazard information to the purchasers of these products.

I also know that there may be some cracks in this, and I trust the voluntary program that industry is bringing forward will fill those cracks.

We intend to work closely with OSHA to make sure that those cracks are filled and that this is a good program.

FDA supports the development and implementation of the OSHA standard and will work with OSHA and other agencies to make sure that the cosmetologists and their clientele are protected from hazardous chemical exposure in the workplace.

In the area of cosmetics, protection of consumers from hazardous or misbranded products depends largely on effective communication; namely, informing consumers and industry about our safety and labeling concerns and working closely with cosmetic manufacturers on these matters. I believe your hearing has catalyzed that type of communication.

We need to inform consumers and industry about our safety and labeling concerns and work closely with cosmetic manufacturers on these matters before they ever become regulatory issues.

To conclude, Mr. Chairman, let me state that it is in keeping with the intent of Congress that FDA programs place responsibility for the safety of cosmetics on industry. Our role is to monitor safety of these products, and as I have noted, other agencies also play a role in this.

It is a good regulatory approach to have multiple agencies working cooperatively together.

There is already substantial authority in the law to support this approach. While regulations can contribute to making products safer, even the most stringent regulatory requirements cannot guarantee absolute safety and quality assurance.

However, quality assurance and safety can be improved with active cooperation among those who make the products, those who use them, and those who regulate them.

Our current laws and regulations are designed to meet these goals.

Mr. Chairman, I would be happy to answer any questions.

[Mr. Young's statement may be found in the appendix.]

Chairman WYDEN. Dr. Young, thank you. Again, let me say thank you for the cooperation that you have shown the subcommittee in trying to accumulate our information needed for this hearing.

Let me recognize my colleague from North Carolina, if he would like any kind of opening statement.

Mr. PRICE. I do not have an opening statement, Mr. Chairman. I do want to commend you for the continuation of these hearings, and I will await a chance to question the witnesses. Thank you.

Chairman WYDEN. We thank our friend and always welcome him, knowing of his long interest in health care issues.

Dr. Young, what I would like to do first is to walk through the powers that the Food and Drug Administration has in this area, and I think some specific questions can be addressed in pretty short order.

Dr. YOUNG. If I can, I will have counsel comment on some of the law that I might not be as familiar with.

Chairman WYDEN. All right. We did not swear him and since he is here as your counsel, I would like to have him continue his role as counsel in terms of advising you, so you can give answers and let us proceed in that—pardon me? We cannot have you both as a witness and as counsel.

Dr. YOUNG. He is a witness, not to advise me.

Chairman WYDEN. All right.

Dr. YOUNG. I have noticed over my 4 years and a couple of months that these laws are a bit arcane, and lawyers talk in different languages than physicians do.

Chairman WYDEN. I think we will find these pretty straightforward.

Dr. Young, it is my understanding that there are no premarket clearance requirements for cosmetics.

Dr. YOUNG. That is correct.

Chairman WYDEN. It is my understanding that there are not any specific statutory requirements that a cosmetic ingredient be tested for safety before it is used in a cosmetic.

Dr. YOUNG. That is correct.

Chairman WYDEN. It is my understanding, Dr. Young, that for FDA to take regulatory action against a particular formulation, the agency has to do so under the misbranding and adulteration provisions of the statute.

Dr. YOUNG. Yes; those are the ones that I indicated on the chart.

I have found that in the case of something like methylene chloride, when we have reached such a decision, we are able to promulgate a regulation on it.

We have done that with some things in bubble bath and other products as well.

Chairman **Wyden**. The burden of proof in showing that a product is adulterated or misbranded rests entirely with the agency.

Dr. **Young**. The burden is absolutely on us. One that we worked on, in the records that I have submitted, is hexachlorophene, which is a good example. We did have the burden of proof. We did take something that had been used for years and show that it was a problem.

Chairman **Wyden**. Now, if the FDA wants to remove a cosmetic from the market for lack of safety, the only way it can do it is to show that the product is harmful.

Dr. **Young**. Yes; that is what we are doing, essentially, in the case of methylene chloride. We are analyzing the information. In that case, we triggered a process by putting out a notice of proposed rule making. Further information came in. We have evaluated that. Now, we are getting close to our final decision.

Chairman **Wyden**. If the agency wants to prohibit the use of a cosmetic ingredient, it has to demonstrate that the ingredient may be poisonous or deleterious under the intended condition of use.

Dr. **Young**. That is correct. With a single exception. If the ingredient is a drug-like compound, for example, the retinoid compound of a vitamin A derivative, such as Retin-A or Accutane, we would have the ability to cross over into the cosmetic field, if it is a drug itself.

Chairman **Wyden**. Is it not true that due to the paucity of information that is required to be submitted to the Food and Drug Administration, the agency finds it difficult to become apprised of safety problems with cosmetic ingredients?

Dr. **Young**. That is a little bit of a gray area. The gray area is that we rely on and get a substantial number of consumer complaints. If a consumer complaint comes in, then we can look at that particular area and we are apprised that way. We are apprised in many ways by consumer complaints and we welcome them.

Chairman **Wyden**. But the companies are not required to turn over complaints.

Dr. **Young**. That is correct. It is a passive surveillance area in which we rely on consumer complaints, and we did that in bubble bath and also in the product that I mentioned in my testimony.

Chairman **Wyden**. Let me say that was the finding of your task force in 1981.

Dr. **Young**. Yes.

Chairman **Wyden**. In 1981, your task force said:

> Because of the paucity of information required to be submitted to FDA, the agency finds it difficult to become apprised of safety problems with cosmetics.

Dr. **Young**. Yes; I would agree with that. I am trying to point out that there is a passive process we rely on quite extensively in gathering information. We look at that peak above the horizon and, if there is a number ~~of~~ complaints, then we look at them. That is the sole way we get that information, unless it is called to our attention.

Chairman WYDEN. Just so we are clear on the record, there have been no statutory changes since 1981 when your task force said that it would be difficult to become apprised of safety problems?

Dr. YOUNG. That is right. Please, I am just trying to say that——

Chairman WYDEN. I understand.

Dr. YOUNG [continuing]. It is the way we look at passive surveillance, and that is why it is a bit gray. We do get this information.

Chairman WYDEN. It is my understanding that manufacturers and distributors are not obligated by law to notify FDA regarding consumer reports of adverse reactions, is that correct?

Dr. YOUNG. That is correct.

Chairman WYDEN. It is my understanding that the companies are not required to send any data or information to FDA regarding product safety, is that correct?

Dr. YOUNG. That is correct.

Chairman WYDEN. It is my understanding that even after banning a specific cosmetic ingredient because it is unsafe, it is difficult for FDA to enforce the ban because cosmetic manufacturers and distributors are not required by law to register their manufacturing establishments or product formulations with the agency, is that correct?

Dr. YOUNG. It is part correct and part incorrect.

It is correct that they are not required to register these by law. However, if a hazardous product was on the market, we could seize it. I have been very pleased to have the media cooperate with us and get out public alerts.

You saw me do this on the tampering and other crises in the United States, and I feel that if there is a problem, I could, through the use of the press, get that information out quite well, but I do not have the legal authority.

Chairman WYDEN. That is an interesting notion of regulation, that somehow the press will be the party responsible for getting the word out, but I do not want to get into that at this point.

Dr. YOUNG. I wanted to acknowledge that they are helpful. Sometimes, in this town, they are excoriated more than recognized.

Chairman WYDEN. We do not question for a moment their role. We would take exception to the idea that they would substitute for a regulatory or oversight function.

But you do not quarrel, though, with the specific finding of your task force again in 1981 that problems with respect to enforcing the ban are made more difficult because distributors are not required to register their manufacturing establishments or formulations, is that not correct?

Dr. YOUNG. They are made more difficult, but I want to point out clearly that if there is an emergency or a significant hazard, I will leave no stone unturned to deal with that product. I have got some bully pulpits to use and have used those in the past.

We do have a voluntary registry, and I will submit for the record the number that participate. I think the participation needs to be improved. We have a number of firms not participating, and you will see in the material I submit for the record that that is something I have spoken to industry about, and I hope that they will address it in their testimony as well. We need a better and more complete registry.

Chairman WYDEN. The only thing that concerns me, though, about your notion of regulations, that you are going to use the bully pulpit, is that it really does not do anything until after the fact, until after there is a problem. My concern is if we do not even know where these manufacturing establishments are located, we really cannot have any semblance of a preventive kind of system.

We will want to discuss whether that should be continued in the future in a bit.

It is also my understanding that FDA lacks the statutory authority to inspect any records regarding safety testing that a manufacturer may have voluntarily performed, is that correct?

Dr. YOUNG. That is true. We do not have the authority, but we can, if the manufacturer cooperates, get the records.

Chairman WYDEN. OK, I will ask a couple of other questions and then I will recognize my friend from North Carolina.

Now, Dr. Eiermann, who runs your cosmetics program? The Director of the FDA Division of Cosmetics Technology, told the subcommittee staff that on many occasions, the cosmetics industry has refused to disclose testing data to FDA, is that correct?

Dr. YOUNG. Yes; to the best of my knowledge, that is correct, and I have spoken with the industry about that, again pointing out that, where necessary, they have to be far more cooperative in that vein.

Chairman WYDEN. Now, reviewing consumer complaints is one important way to monitor trends in adverse health effects from various cosmetics products, is that not right?

Dr. YOUNG. Yes; that is true.

Chairman WYDEN. How then can we establish a baseline on cosmetic hazards if we do not have that kind of information?

Dr. YOUNG. I think that I should explain a little about adverse reaction reporting, and to contrast drugs and cosmetics, if I could.

The law does require, in the case of drugs, that if there is an unexpected death, the report be turned in within 5 days or fewer. In the case of unexpected serious illness, about 15 days or fewer. That is because, by and large, the adverse reactions in medicines are much more significant than with cosmetics, which were judged by Congress to be safe by comparison to drugs.

For cosmetics we use a passive system, which is a system that you are describing. We also use a passive system in food. That gives us only those large spikes above the background to identify a problem. You might ask what the impact of a mandatory system is.

I have found that in 4 years we have been able to combine the routine reporting with the physician's understanding and communication, and complaints from consumers. So, I have found I do get a lot of information from consumer complaints, and I do not want to leave the impression that it is not a highly valuable point of focus. We welcome people reporting problems with cosmetic use.

Chairman WYDEN. I think one of the things that concerned me after our hearing was the summary that Mr. Eiermann gave of your program. He said:

> If we do discover that an ingredient is dangerous, all we can do is get out and beat the bushes, make it known to the cosmetics industry, and stimulate their voluntary action.

Is that not essentially the description of a toothless tiger?

Dr. YOUNG. No; not to that extent.

Chairman WYDEN. You disagree with what——

Dr. YOUNG. I disagree——

Chairman WYDEN [continuing]. Mr. Eiermann said?

Dr. YOUNG. I would disagree with only parts of it. I think he has made some good points, but the points that I would disagree are these: I have found in 4 years that when we have had a problem—I will give you the example of Retin-A—we have been able to work very extensively with our enforcement inspectors to examine manufacturing sites and to pull products off the market.

Remember, we look at products on the market itself. I have used the bully pulpit of the media in other ways. So, it is more than just sitting back there and wringing your hands and saying nothing can be done.

Chairman WYDEN. Again, that is talking about a completely different regulatory approach in that area.

To sum it up, you have essentially treated the product as a drug, and you can move expeditiously, but what Mr. Eiermann is talking about is products that are not drugs—cosmetics. I wonder if you do disagree with his statement.

Dr. YOUNG. I would say that, if it is harmful, we can move rapidly and deal with it. We would have to prove it, but we would be able to deal with it. In particular, as long as we work on it and can establish this, I think we can deal with it effectively.

Chairman WYDEN. You and I have talked on many occasions about the resources question, and I am in great sympathy with your concern in this area and I believe that Congress is going to have to do more to get the kind of quality services that are needed.

But it is true at present, FDA has provided fewer resources to the cosmetics program than the other programs, is that not correct?

Dr. YOUNG. Unquestionably; that is why I said I am pleased that I have increased it by 25 percent. We went from $2,647,000 and 26 employees in 1984 to 33 employees and $3,417,000, but that is small.

Our problem, and I do not want to raise false expectations here in the minds of the people in the Nation, is that we are dealing with other overwhelming problems, such as AIDS.

I will be holding my own hearing this afternoon on salmonella in eggs. Some of the issues that we are focusing on are critical devices, and problems in food, and we have had to set priorities.

So, cosmetics have been a lower priority, but the products on balance are safer than some of the others we regulate.

Chairman WYDEN. If the agency were given more statutory authority, would more resources be committed to overseeing cosmetic safety?

Dr. YOUNG. Only if the resources were provided to the agency.

Right now, we are cut thin. We have a great problem, looking at fiscal year 1989. As you know, Mr. Chairman, the House has recommended appropriations of 1 percent below the President's Budget and the Senate, 2.7 percent below. We would be looking at furloughs from the agency if we were to drop $17 million below our expectation. I would not want to promise we would do more. It would be a fraudulent promise and a false, deceitful hope, to have that expectation.

Chairman WYDEN. Dr. Young, is it not correct that there is very little information available on the potential or identified long-term chronic health effects that the chemicals in these cosmetics can cause?

Dr. YOUNG. Some of them have long-term effects, not studied primarily in cosmetics, but in other particular——

Chairman WYDEN. Let me ask you specifically about cosmetics because we heard testimony from experts at our last hearing, experts close to the industry, that there is very little information available with respect to long-term analyses of the effects that the chemicals in cosmetics can have on people, is that not correct?

Dr. YOUNG. That is correct. We would have this information only if it were available through studies which relate primarily to other uses of that chemical. Then we would have to balance the amount used with the site of delivery and its rate of absorption and come up with an estimate. But there is no premarket approval.

Chairman WYDEN. I am talking about something else. I am talking about research here. Are you concerned about the lack of information that is available on the long-term health effects that chemicals in cosmetics can have on people?

Dr. YOUNG. In general, whenever you are dealing with a potentially toxic chemical, you have to do a risk assessment to see what the risks are. Compared to all of the other crises that we are dealing with, though these are significant questions, we do have others that are driving the agency a bit more. Pesticides in food, and some of the issues that we have had with toxic chemicals in food are examples. We are not quite at the same level of concern with cosmetics, but, yes; these compounds could be potentially harmful. We do need to know as much as possible about them.

Chairman WYDEN. You do then think that this is a significant health question as it relates to the long-term effects?

Dr. YOUNG. That is a very difficult question. You would almost have to answer it product by product. There are some products where we might have concern, but we are less concerned in cosmetics than we are with any of the other products that we regulate.

Chairman WYDEN. Let me ask you about this then. We asked the industry to give us a list of 2,983 chemicals that were used in cosmetics. It was given to us by the industry, which, I might add, has been most cooperative in working with the subcommittee in a general fashion. They gave us this information, in particular.

Now, we asked the National Institute of Occupational Safety and Health to analyze those 2,983 chemicals, and they went out and compared those chemicals with their registry of toxic chemicals. What they found was that 884 cosmetic ingredients had been reported to the Government as toxic substances.

Now, obviously, that has not been followed up, and we do not know specifically what the health implications are, but that certainly concerns me. Does it concern you?

Dr. YOUNG. Yes; knowing of your concern I pulled a list from our Parklawn computer and crosschecked it. We had great cooperation from the National Institute of Occupational Safety and Health. There are a couple of caveats that I would like to mention, and then I would like to look at the list in a little detail to answer your question and advise you on it.

The important thing to realize about this list is that this is a compilation from the literature.

Chairman WYDEN. That is why we said specifically that this information has been reported to the Government.

Dr. YOUNG. That is right.

Chairman WYDEN. The Government has not done an analysis. But, frankly, that is one of the things that most concerns me about this field, that until somebody goes out and digs up this information, these are not even issues to be analyzed.

We are saying nothing other than, based on what scientists have reported to the Government that of these 2,983 chemicals, a significant number have been reported as toxic substances, and I think before you get into this in detail, what I would like to ask first is, is it the plan of your agency and NIOSH to follow up on this?

Dr. YOUNG. I think it would be honest to say that FDA can look at some of these which we think are more significant. We can cross reference these, and, we do have a small research program that Heinz Eiermann is responsible for.

Also, it would be fair to say that we could look only at the most significant ones. In toxicology studies, we are devoting about $1 million per study. These are done by the National Toxicology Program [NTP].

The Food and Drug Administration identifies compounds that we are concerned with and turns the information over to NTP; then they do the chronic studies. That is the mechanism of handling it.

The most important thing for me to mention is the portion in the introduction to these studies, which says:

> Under no circumstances can the toxic dose values represented with these chemical substances be considered definitive values for describing safe versus toxic doses for human exposure.

That is exactly why you need the research to determine what the toxic levels are, if any.

Chairman WYDEN. You made the point. We need this research, and it is not being done, at least it was not being done as of last week, and the reason I bring it up today is only by way of saying that what we have seen today indicates that there better be some Government followup.

Dr. YOUNG. Sure.

Chairman WYDEN. Is there going to be?

Dr. YOUNG. It really will depend in part on the funding level, but two things are very important for you and the public to understand.

I was very pleased when we recruited a new director of the Center for Drug Evaluation and Research. Dr. Karl Peck is an internationally noted individual with expertise on skin penetration and absorption, and he will be working in collaboration with Dr. Robert Scheuplein, Center for Food Safety and Applied Nutrition, who is also noted for his toxicology expertise. We intend to develop a major program on skin penetration when we move into our facility in Module 1. We again would have to set priorities. There is no way that we could look at all 884 substances.

Chairman WYDEN. Absolutely not. We would like to have the Government make a commitment to look at the priority areas because this indicates—I mean, it really screams out to me for follow-up. That is all we are talking about.

Dr. YOUNG. The priority areas can be looked at and will be looked at as funds permit us to do it because of our interest in skin penetration in general. Some of the compounds on the list, as you know, are as simple as vinegar—acetic acid—which is listed as having three cases of acute toxicity.

Chairman WYDEN. Right; when would you anticipate following up on this to look at the priority cases?

Dr. YOUNG. I must say honestly that it is going to depend on whether the President's budget is met in the next year. If we fall below the President's budget for the Food and Drug Administration, we are going to be scrambling, and I would not want to be held to a commitment.

Chairman WYDEN. If you get the funds proposed in the President's budget, can you begin an analysis of these toxic substances?

Dr. YOUNG. I would ask Heinz Eiermann to see whether he can make a priority list of the ones that are most important. We do have four people who can be devoted to this.

Chairman WYDEN. What I would like to ask you, and I would like you to pursue this in cooperation with the industry, that you work with the industry and with this subcommittee and get back to us, let us say, within 30 days on a plan to begin this undertaking for the priorities.

Dr. YOUNG. If you have the budget passed in 30 days and it is signed, I will be happy to provide the plan.

Chairman WYDEN. Let us say that we would like to see the plan and then I can use the plan to go out and get the resources.

Dr. YOUNG. I was afraid you would say that.

Chairman WYDEN. We know that this is chicken and egg, and you make a very valid point. It is one you know I happen to agree with.

Dr. YOUNG. Yes; I do know that, and you have been very supportive.

Chairman WYDEN. Let us have you work with the industry to put together a plan to begin to follow up on these priority cases and then let me wage the budget fight because——

Dr. YOUNG. I think the approach that you are taking is a very critical one because industry needs to be able to work cooperatively with the agency. They have the resources. They have the information, and if we can pull that into the agency and reallocate some of Heinz's time, I think we can come up with at least an outline of what we would do. It would take more than 30 days to get a comprehensive plan, but we can get you an outline of what our thoughts would be.

Chairman WYDEN. One last question and then I want to recognize my colleague. It sounds like the industry's program is a step in the right direction, and you have spoken with me as well about your concern with respect to the workers.

Dr. YOUNG. That is right. I really want to see this done properly.

Chairman WYDEN. Is it not correct, as public health policy, that health problems that are first found with workers very often turn up in the general population as a whole? You said yes?

Dr. YOUNG. Yes; while I was dean of the medical school, we tried to build a program of occupational health because it covers a large group of individuals. We can look at diseases that occur in the workplace and people who are ill. It is a complicated area. We have not had as much emphasis on occupational health as I feel, as a physician, would be appropriate throughout the Nation.

The medical schools, in their curricula, have moved a bit away from that. I would call very specifically on the record for a greater attention to occupational health. I do not think that is a governmental role, but there can be some increased educational and medical practice attention. I believe that would be in general support.

Chairman WYDEN. I only bring it up by way of saying that this may highlight some of our concerns. It does not divert the subcommittee's interest from the population at large because it is my understanding, and I appreciate your saying you would agree, that as a matter of public health policy, very often problems you see with workers turn up in the general population as a whole because the workers are the first to experience it.

Dr. YOUNG. That is right.

Chairman WYDEN. If you are a cosmetologist, you may use the product, of course, a tremendous amount in a very short period of time, but if you are a consumer, you may use the same product, also a tremendous amount over a longer period of time. It is possible that what we learned from analyzing worker health problems can help prevent problems with the general population as a whole, isn't that right?

Dr. YOUNG. That is right. A good example of that was with the workers who used to paint the radium-containing dials on watches. That was a problem a number of years ago, but it was found first that the individuals who licked the brush, painted the dial, and then ingested small amounts of the luminous material, which was radioactive, got illnesses. That was a sentinel point.

I could give you example upon example where toxic exposure in the workplace gave good examples of where we are going. That is why I am so interested in cooperating with OSHA, to see what we can do to minimize those. I am pleased to have learned of their recent regulatory action.

Chairman WYDEN. I will have some additional questions in a minute, Dr. Young. I want to recognize my friend from North Carolina.

Mr. PRICE. Thank you, Mr. Chairman. Thank you, Dr. Young, for appearing here today and for your responsiveness to the subcommittee's concerns.

As you know, it was almost 10 years ago that the Congress received a report from the Comptroller General which recommended that Congress should authorize the Food and Drug Administration to require cosmetic manufacturers to prove the safety of their products. In that report, the FDA Commissioner of that time was quoted in congressional testimony to say the following:

> As the law stands, cosmetics are the only products for which the legal burden rests on the Food and Drug Administration to prove a hazard to the public rather

than on the industry to demonstrate their product has been tested in accordance with currently-accepted methodology and that it is safe.

Is there anything that has occurred in the last 10 years to essentially alter that conclusion?

Dr. YOUNG. No; there has not been anything that changes the conclusion because the law has remained unchanged.

The only thing that I would add to that is that in its wisdom, Congress, when it passed the Federal Food, Drug, and Cosmetic Act, recognized that cosmetics were the lowest of the hazards, and I would still confirm that point.

The issue in the United States is we are dealing with competitiveness. With a finite amount of resources, where and how do you best expend regulatory efforts? I think that is an issue that one needs to address.

I believe that cosmetics are safer than other products we regulate. I believe that we do have the authority and regulation to deal with this, but I also believe that it requires a large degree of cooperation with industry in view of the statements that you just read.

Mr. PRICE. Your statement about the allocation of scarce resources, though, is not precisely responsive to this recommendation.

Dr. YOUNG. No; well, yes and no. In the sense of scarce resources, I have increased them by 25 percent. Not knowing in 1984 that there would be a hearing, it was a direction which you saw this Commissioner going.

On the other hand, you also have seen me worrying about the blood supply in your State. We inspected the Red Cross in Raleigh, NC, and some other places, and yesterday signed a voluntary agreement with the Red Cross, which I think meets these issues.

Given the balance of the terrible issues with AIDS and the concern about Alzheimer's disease and some of the other things that we focus on, we have put cosmetics at a lower priority. That is fundamentally true.

Mr. PRICE. Let me pursue the particular question of inspections and the kind of authority that you have. You do have the statutory authority to conduct inspections of cosmetic establishments, is that true?

Dr. YOUNG. Yes; we do, and I have focused particularly on imports, where I have been concerned as well.

Mr. PRICE. FDA reported to the subcommittee that, of 20,000 inspections done in fiscal year 1987, only 213 of these were done for cosmetic manufacturers; that is, around 1 percent.

Dr. YOUNG. That is correct.

Mr. PRICE. That does seem like a rather small number of inspections for an $18.5 billion a year industry.

Dr. YOUNG. Yes; but, again, Mr. Price, it really depends on the priority. As I said recently, I came to Congress and said that I had a great concern. I was supported on this in developing increased inspections—doubling the inspections—of blood banks. I try to deal with the priorities in relation to public health needs. Cosmetics are much safer products than some of the others that we deal with.

You also saw me focus on imported cheese. For a period of time, 80 percent of the Brie cheese coming into the United States was not allowed to come in because of contamination with listeria monocytogenes. That is the single most hazardous organism, a pathogenic organism, with a mortality rate of 25 percent.

We focused on where major public health problems lie. By and large, if important problems are there in cosmetics, we do want to look at them, and have tried to match the inspection and surveillance resources with the degree of the problem.

Now, I have been increasing the field force in the Food and Drug Administration year by year because I want to increase our enforcement. You have seen a large number of enforcement actions by FDA in the last 3 years. We do not want to go to sleep on this, but it is not quite the priority that some of the other demanding issues are.

Mr. PRICE. I understand that. I would like to focus, though, on exactly what these inspection visits are aimed at, and exactly what the priorities are within this program. You do not have a specific surveillance program to collect cosmetic samples to monitor for safety, is that right?

Dr. YOUNG. We do collect some. We look for things, such as bacteriological contaminants. We would look also for debris within the cosmetics. Most of the detentions that we made last year were on the basis of sampling.

I do not have the exact numbers. I will provide them for the record, but I believe we did about 364 samplings on the detentions that we had last year on cosmetics.

Mr. PRICE. The focus of these samplings and of the visits is on sanitary conditions? Is that fair to say?

Dr. YOUNG. We look at sanitary conditions. We look at labeling, and based on this we may analyze products in the laboratory. Mr. Ronk reminded me that in the case of consumer complaints, we may or may not do animal studies. I know particularly, when I was dealing with colors, that I asked the agency to look at colors that were illegal, and we found that a number of imported products contained colors that were banned in the United States. We went after those, and those involved laboratory studies as well.

Mr. PRICE. So, the kind of failures your inspection teams might uncover would be unsanitary conditions?

Dr. YOUNG. Unsanitary conditions.

Mr. PRICE. Possibly unapproved color additives?

Dr. YOUNG. Unapproved color additives. We probably also would pick up contamination of the product by particles or problems in the packaging itself that might lead to bacteriological contamination. We would not pick up long-term chronic effects. We do not do long-term chronic bioassays.

Mr. PRICE. False or misleading labeling, might you catch that?

Dr. YOUNG. False or misleading labeling is the easiest, particularly in those that are language problems.

Mr. PRICE. So, those inspections really cannot help you determine whether or not the products are safe, except they might identify batches that are contaminated or use unacceptable colors?

Dr. YOUNG. They take the tip of the iceberg. Let me go back to methylene chloride, for example. If we apply the regulation there, if we judge that this is a compound that should not be in the marketplace after a certain time, then I would send the inspectors out and see whether there are products that violate the regulation and remove them by either recalls or seizures.

Mr. PRICE. This focus on color additives, what is the rationale for that? Do these additives pose greater health hazards than other kinds of cosmetic ingredients?

Dr. YOUNG. In our law, we have, for color additives, premarket approval requirements. That is one part of cosmetic regulation that is different. In that case, we are looking to see whether cosmetics in the United States that are not approved and are shown to violate are either imported or include domestic-produced colors.

Mr. PRICE. So, the reason for that focus has as much to do with your statutory authority as it does with any objective assessment of where the hazards lie?

Dr. YOUNG. Yes; it does, although I would say our concern has been generated about some particular areas of the body, and particularly around the eyelids. We have been concerned about potentially toxic colors.

Mr. PRICE. There is no question that in terms of the statute, you have more authority to protect consumers against potentially dangerous colors than other——

Dr. YOUNG. Yes; we do.

Mr. PRICE [continuing]. Kinds of hazards.

Dr. YOUNG. No question.

Mr. PRICE. How many cosmetic product seizures has the FDA made?

Dr. YOUNG. Let me ask Mr. Ronk whether he knows.

I would have to submit that for the record. If my Center Director does not have that memorized, then I certainly do not. I will get that for the record for you.

Mr. PRICE. Any kind of estimate? Any kind of rough figure we could have on that?

Dr. YOUNG. It is not very many, but I can get that for the record. I am sorry.

Mr. PRICE. That would be helpful, if you could supply that for the record. I appreciate your responses to these questions. I would have to say it does not sound like a very vigorous enforcement effort. However, it also sounds as though at least part of the explanation for that is the kind of statutory authority that you have, and also, of course, the budget constraints that force you to make some very painful choices in terms of priorities.

Dr. YOUNG. Yes; it is those two and the relative safety of the products that really drive it in this direction.

Mr. PRICE. Thank you, Mr. Chairman.

Chairman WYDEN. That does not make me have a lot of confidence in the program to deal with seizures when there are contaminated products, that the information is in the district offices and nobody here from the agency knows about them. But we will hold the record open on that.

Dr. YOUNG. Please do not look at it with a lack of confidence. It is merely a difficulty in the entire program to have every detail at your finger tips. The number of seizures is not something that I know exactly, and I do not want to give you a figure that would be misleading.

Chairman WYDEN. Let me ask you one other question about the inspection issue that I found important.

In response to the questions from the subcommittee, the FDA told us in their written response that when the agency inspects cosmetic manufacturers, that, "The agency usually discovers absence of safety substantiation at the time a product is found hazardous."

Now, at the very least, that raises a pretty serious question about the existence of adequate testing data, does it not, Dr. Young?

Dr. YOUNG. The testing data is an issue that I also have raised with the industry to be sure that they are more responsive in supplying this type of data.

We cannot test every one of these compounds. It would be impossible for us to do it, but if there is quality control information, quality assurance information, as you also asked for, Mr. Price, we may need to get that, particularly on products that we are very concerned about.

Chairman WYDEN. What I am concerned about is that you cannot get good industry data in order to really make an assessment as to whether the product is safe.

I mean, if your people are saying, as they did in their written response, that there is generally an absence of safety substantiation when they go out to try to determine if a product is hazardous, that basically says we do not have much of a system for getting adequate testing data, is that not correct?

Dr. YOUNG. That is correct. On March 3, 1975, FDA published a regulation to deal with that. It said that FDA established the labeling of cosmetic products for which adequate substantiation of safety has not been obtained. Each ingredient in each finished product must be adequately substantiated for safety prior to marketing. Any such ingredient or product whose safety is not substantiated prior to marketing is misbranded unless it contains the following conspicuous statement on the principal displayed panel, and I emphasize now, "WARNING: The safety of this product has not been determined" (21 CFR 740.10).

Chairman WYDEN. But that deals with labeling, and your people said—I gather you put that out a number of years ago?

Dr. YOUNG. Yes; 1975.

Chairman WYDEN. Your people told us, "There is an absence of safety substantiation at the time a product is found hazardous." I really think that is an area where we are going to have to do some work, Dr. Young, because what it says is that there is not an adequate testing program out there, not a testing program by you, not by the industry, because when you go out there, you cannot then get the substantiation you need.

Dr. YOUNG. I would like to revisit this, and I will take into account all of the testimony that you receive at this hearing and will be delighted to follow up and work with you on strengthening this, because we do put safety first. We do not want to have holes in our net.

Chairman WYDEN. Let us pursue that vigorously because that is the finding of your own people. That is not something that——

Dr. YOUNG. We discussed, in preparation for this hearing, that this was a problem area. I did bring this to the attention of the industry and pointed out that, as far as I am concerned, we need much more safety information and have access to that material. I think I can get it voluntarily.

As you know, the FDA does a number of things voluntarily and voluntarily sometimes is in quotes, and we will work vigorously on this.

Chairman WYDEN. You talk about the voluntary program, and I note in your prepared remarks that you gave, that in most of the categories on voluntary filings——

Dr. YOUNG. Yes.

Chairman WYDEN [continuing]. Formulations and things of that nature, under 50 percent of the firms have made a voluntary finding. For example, with respect to filing and amending formulations, since 1984, only 14 percent have filed.

Dr. YOUNG. Yes.

Chairman WYDEN. How can you make a voluntary program work if only a small fraction of the people will participate?

Dr. YOUNG. I told the trade association, and I hope you will ask them to confirm this, that this type of a voluntary compliance is unacceptable, improper, and will not be tolerated.

Chairman WYDEN. What are you going to do to turn it around? Are you prepared to tell the industry that if they do not get those voluntary filings up, that you are going to come up to Capitol Hill and we are going to make some requirements that they do it?

Dr. YOUNG. I think this hearing has received a lot of attention, Mr. Chairman.

Chairman WYDEN. I am hopeful. I would hope, Dr. Young, that you get that message to the industry because we are going to pursue this in a cooperative way with your agency, and it has always been my preference, as you know, I sit on the principal regulatory committee in the House.

Dr. YOUNG. Yes; I know that.

Chairman WYDEN. The Commerce Committee has the responsibility of regulating in the public health area. We try to make things work in the private sector first. It is easiest, it is most expeditious.

Dr. YOUNG. That is correct.

Chairman WYDEN. But the last part of your testimony with respect to voluntary filings does not exactly stimulate confidence in the voluntary system.

When you have only 14 percent of the firms making voluntary filings, that is not much of a voluntary program. I am glad that you told the industry in very direct terms that you expect marked improvement in that regard, and I hope that you will also get the message to them that you are not going to wait forever on this, because my feeling is that if they do not act voluntarily on these things, then Congress ought to think about making sure that it gets done.

Dr. YOUNG. It is no accident that I attached that to the back of my testimony, Mr. Chairman. I believe the industry might even be sitting in this room today, and I hope they heard both of us.

Chairman WYDEN. All right. I suspect that all those things may be true. Dr. Young, let me ask one or two questions about the antiaging cream situation. Now, you said that 30 percent had modified their claim.

Dr. YOUNG. That was not relative to Retin-A. This is on the drug claims on cosmetics in general. The creams that you slather on your face and they dissolve your aged cells while you sweat; a remarkable claim.

Chairman WYDEN. Yes.

Dr. YOUNG. It was Dr. Bernard's claim, if you remember, when he got on the telly and told how you could sleep your age away.

Chairman WYDEN. Thirty percent you said have changed their claims, but what about the other 70 percent?

Dr. YOUNG. We are prepared, if this problem continues, to go out and make seizures.

Chairman WYDEN. When would we be at that point? How much longer are you going to give companies to make those voluntary changes?

Dr. YOUNG. Mr. Taylor and I have forwarded those in the appropriate legal channels, to the best of my knowledge. Tom, can you speak to that?

Mr. SCARLETT. There are seizure actions in preparation within the agency.

Dr. YOUNG. I do not think that we can go any further than that, Mr. Chairman——

Chairman WYDEN. No, no; I understand.

Dr. YOUNG [continuing]. At this time.

Chairman WYDEN. So, from 30 percent, you received modified claims, and you have told us today that the agency has initiated proceedings for seizures on others that have not modified?

Dr. YOUNG. We better not pursue that, but Max Schmidt, one of the earlier Commissioners, said FDA is an educational institution and the slow learners learn in jail.

Chairman WYDEN. Has FDA ever tested any of the Retin-A that has been seized by the Customs Department to determine if the product is bogus, Dr. Young?

Dr. YOUNG. Yes; we have. In fact, one of the things that happened when I was doing an interview about this, was that the interviewer brought in some compound that she was able to get from a physician and we analyzed it. In that case and others that we have analyzed, there was one-fifth the concentration that was therapeutic. That is about as good as putting water on your face. It is not going to have much effect at all. The good news is that it is ineffective. The bad news is that it could have some consequences.

Chairman WYDEN. Where is the bogus material coming in from?

Dr. YOUNG. It is coming in from chemical supply houses. What usually is done is that a person who is manufacturing this illegally buys it under the generic name, puts it into a salve that has been bought in a bottle from another place, mixes it in a garage or some other place, and then ships it across State lines. That is irresponsible and illegal, and I will submit for the record for you the enforcement plan that we have out there. I also must say, without going any further, that we have actions on this as well.

Chairman WYDEN. Dr. Young, you confirmed what Dr. Eiermann told the subcommittee staff, that the industry on many occasions has refused to disclose testing data to FDA.

What do you think should be done about that? Do you think that it is time for statutory change that would stipulate that when the FDA believes it is in the public interest, in the interests of public health, that cosmetics companies would have to turn over test data to you?

Dr. YOUNG. At this point in time, my judgment is that I would like to give one more try to the voluntary compliance, because of our other priorities, and because I feel if we can get the private sector to do it, it should be done there.

I have put them on notice that I felt it was inappropriate not to provide this information to FDA when requested. I hope that in their testimony today, which I have not analyzed, they will pick that up. I have discussed it with them recently and pointed out that my expectations are that these safety data must be supplied when appropriately requested by FDA, because that meets the public trust and meets the public health responsibility.

Chairman WYDEN. Well——

Dr. YOUNG. I would be interested in their testimony as you ask them that question, I hope, as well.

Chairman WYDEN. It will come up, and I must say I have very little patience on this particular point. I think we are going to have to have some public interest requirement that when you all feel you need to see test data, you must be in a position to do it, particularly since your agency supplied us with the information indicating that when you do have a problem, there is no information out in the field to really substantiate these safety issues.

I appreciate your willingness to look carefully at this, and I have no quarrel with the idea of giving the agency another opportunity, but I am not going to have extended patience on this point.

You have been very helpful, Dr. Young. I think more than anything, this subcommittee has been involved in a learning exercise, and you have filled in quite a few gaps. I made a little checklist of the kind of limited powers that you all have. No premarket clearance of cosmetics. No statutory requirements that an ingredient be tested for safety before it is used.

The companies do not have to send test data to you for product safety. Companies do not have to tell you about consumer reports of adverse reactions. We do not even know where these outfits are because they do not have to register their establishments.

There are a lot of gaps out there. Certainly, we want to see as many changes made voluntarily as we possibly can, but I think it is time for all of us, the Congress and the regulators, to get more involved in assessing what this industry is all about, because to think that we do not have, for example, a study that really tells us about the long-term health effects of these products concerns me greatly.

These products, after all, are chemicals. Cosmetics are combinations of chemicals, a number of which, based on this new study that we received today, have been related to toxic substances.

Now, I think what we need to do is rather than rush and panic, we need to move quickly to do some followup. I sense that you want to pursue that as well and I want to thank you for your cooperation. We will be working with you in the days ahead.

Dr. YOUNG. Thank you. I will vigorously pursue the voluntary approach on this and report to you and give you the progress of what we have been able to accomplish.

Chairman WYDEN. Thank you. Unless you all have anything further you would like to add, we will excuse you at this time.

Dr. YOUNG. Thank you.

Chairman WYDEN. Our next panel, Dr. Charles Adkins, Director of Health Standards, Occupational Safety and Health Administration, and Mr. William MacLeod, Director of Consumer Protection, the Federal Trade Commission.

Mr. MacLeod and Mr. Adkins can come forward.

Gentlemen, we welcome you to the subcommittee. I believe you have been here through our proceeding.

It is the practice of our subcommittee to swear all witnesses.

Mr. Adkins and Mr. MacLeod, you will be appearing as witnesses and your associates as counsel today?

Mr. ADKINS. Ms. Silk will be a witness. She will be answering questions, also.

Chairman WYDEN. Ms. Silk will represent your agency as a witness.

Mr. ADKINS. Yes.

Chairman WYDEN. Mr. MacLeod, the gentleman who is on your——

Mr. MACLEOD. Mr. Peeler, my Associate Director for Advertising Practices, may also have some information of value to the committee.

Chairman WYDEN. All right. Do you desire to have him testify as well and be available for questions?

Mr. MACLEOD. Yes.

Chairman WYDEN. Do either of you two individuals have any objection to being sworn as a witness?

All right. Please rise and raise your right hand.

[Witnesses sworn.]

Chairman WYDEN. We welcome you. We will make your prepared remarks a part of the hearing record in their entirety.

There is always a human urge, almost a biological mandate to read your testimony, and if I could ask you, particularly since we have gone over with our first panel, if you all could summarize your principal concerns, we could have some time for questions, that would be very helpful.

Dr. Adkins, let us begin with you.

Mr. ADKINS. Yes; sir, Mr. Chairman, and members of the subcommittee, it is not Dr. Adkins, I do not hold an M.D. degree or a Ph.D. degree.

Chairman WYDEN. All right. You are a Mr. on that tag and a Dr. up here. We appreciate the correction.

## TESTIMONY OF CHARLES ADKINS, DIRECTOR OF HEALTH STANDARDS PROGRAMS, OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION, U.S. DEPARTMENT OF LABOR, WASHINGTON, DC; ACCOMPANIED BY JENNIFER SILK, HEALTH SCIENTIST, U.S. OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION

Mr. ADKINS. We thank you for the opportunity to testify before you today, and as indicated, I am Charles Adkins, the Director of Health Standards Programs for the Occupational Safety and Health Administration, and I have with me at the table Ms. Jennifer Silk, who is an OSHA Health Scientist.

Our agency shares this subcommittee's concern over potential health risks to employees exposed to cosmetic products at work. We appreciate the information you have brought to light on this issue in the course of these hearings.

I would like to, if I could, describe a little bit of OSHA's overall responsibility for workplace safety and health.

As you know, the Occupational Safety and Health Act was signed in 1970, and the statute grants the agency broad authority to promote safety and health of employees on the job.

Our authority extends to private sector employers with one or more employees. The act authorizes OSHA to establish occupational safety and health standards, conduct inspections, to enforce standards, issue citations and propose penalties for violations of the law.

It also authorizes OSHA to require employers to abate those hazards, provide for training and education, and encourage employee-employer cooperative programs to reduce workplace hazards.

Thus, OSHA has a wide range of tools to use in preventing occupational hazards. In addition to the Federal program, we have 20 States and 2 jurisdictions who conduct their own comprehensive federally approved safety and health programs. Two additional States, Connecticut and New York, operate partial plans in that they only cover State and local government employees.

There are a number of standards which OSHA uses to control hazards in hairdressing establishments and other workplaces where employees may be exposed to cosmetic products.

We have first the 5(a)(1) clause of the OSH Act, which requires employers to furnish a place of employment free from recognized hazards.

Then, we have an exposure-limit table that lists over 400 chemical substances with contaminant levels that employees cannot be exposed over. A number of these substances, such as ammonia and others, are in cosmetic products.

We, in addition, enforce 24 comprehensive standards, including formaldehyde, ethylene oxide, asbestos, and vinyl chloride.

We have recognized for some time that this substance-by-substance approach leaves something to be desired and is not sufficient to address the thousands of chemicals in the work places, and in 1983, we took the dramatic step forward in addressing these hazards when we issued the Hazard Communication Standard.

This standard covered over 500,000 chemical products and substances found in work places. It provides workers exposed to hazardous chemicals with a right to know the identities and hazards of chemical substances as well as to know the appropriate means to protect themselves from adverse effects.

Any chemical that poses a physical hazard or a health hazard is covered by this rule. Employers are required to prepare a simple written program with a list of the chemicals in the workplace, to maintain labels on containers, obtain and maintain material safety data sheets on these hazardous products, and train employees.

The Hazard Communication Standard is a dynamic standard in nature. As new chemicals are introduced to the workplace, the new information about these chemicals becomes available and producers must update the information they provide.

Since 1980, when OSHA published the Hazard Communication Standard or labeling proposal, as it was then known, the intent was to focus the new landmark regulation on the industrial sectors where illnesses and injuries from chemical exposures were most prevalent.

The standard, as issued in 1983, applied only to the manufacturing sector. Employers in that sector were given 2½ years to come into compliance with the standard.

The standard had been in effect only a little more than a year when, in August 1987, we revised the standard to cover all work places, including beauty salons, barber shops, and other establishments where cosmetics are used.

As I said, this standard requires all manufacturers and importers to review scientific evidence on the hazard of the chemicals which they produce or import, and then they must inform employers downstream of these hazards and the employer must inform the employee.

Manufacturers and importers must ensure that each container of a hazardous chemical is labeled, tagged, or marked with the identity of the chemical, appropriate hazard warnings, and the name and address of the manufacturer.

The label or tag must be retained on the container when it is used in the workplace. Labels must be legible and they must be prominently displayed.

Manufacturers, formulators, and importers are required to develop a material safety data sheet for each chemical or substance which they import or produce and then that must be provided downstream. Each material safety data sheet must include information concerning the specific chemical identity of the hazardous substance and the common names of the substance.

It must also provide information about the physical and chemical characteristics of the substances and any known acute or chronic health effects, exposure limits, evidence of carcinogenicity, and emergency and first aid procedures, and the identification of the organization responsible for preparing the MSDS.

Since 1987, September 1987, manufacturers, importers, and distributors have been required to send MSDS is on hazardous chemicals which are supplied to downstream employers in all sectors, including hairdressing establishments and other work places.

The standard contains a requirement for educating employees. Employers are required to establish a training and information program for workers exposed to the hazards. The training and information must be provided at the time of initial assignment and whenever a new hazard is introduced into the workplace.

Employees must receive training on how to read and interpret information from the labels or an MSDS. They must be told about methods of detecting the presence of chemicals.

We are currently enforcing this standard vigorously. In the year 1987, the agency cited 19,674 violations of this hazard communication rule.

OSHA's enforcement of existing permissible exposure limits, or PEL's, will be dramatically improved by its current project to update revised limits. We have a PEL Program underway where formerly we had approximately 400 chemicals in our Table of Exposure Limits. We are updating the existing limits and adding a couple hundred more chemicals.

So, as a result of the permissible exposure limit project, which we plan to have published as a final rule in December, we will have some 600 air contaminants in that table.

One important way OSHA assists employers, particularly small business employers, in protecting their employees is through the on-site consultation program. We have State consultants funded by the Occupational Safety and Health Administration who offer free consultation to employers upon request, and this occurs in every State in the Union.

Since 1975, State consultants have visited more than 270,000 work places and more than one and a half million hazards have been addressed under this program.

I would like to emphasize that OSHA has put in place the mechanisms and requirements to protect employees in the cosmetics industry. We have set numerous standards as well as substance-specific exposure limits and are improving them. The Hazard Communication Standard provides employees with the information to recognize and protect themselves against hazards. OSHA offers assistance to employers through its consultation and education programs.

If these mechanisms are not sufficient, employees may submit a formal complaint to OSHA when confronted with serious work hazards.

We believe that the multifaceted effort, which I have described, is protecting workers in the cosmetic industry.

I should indicate that this Hazard Communication Standard, or re-emphasize, that the Hazard Communication Standard in the last year has been republished to include all sectors in industry and not just the manufacturing sector, as it originally was published.

Mr. Chairman, that concludes my statement on OSHA's efforts to protect employees exposed to cosmetics products, and we will be happy to answer any questions that you might have.

[Mr. Adkins' statement may be found in the appendix.]

Chairman WYDEN. Mr. Adkins, thank you, and we appreciate your participation.

Mr. MacLeod.

## TESTIMONY OF WILLIAM MacLEOD, DIRECTOR OF CONSUMER PROTECTION, FEDERAL TRADE COMMISSION, WASHINGTON, DC; ACCOMPANIED BY C. LEE PEELER, ASSOCIATE DIRECTOR, FEDERAL TRADE COMMISSION

Mr. MacLeod. Thank you, Mr. Chairman. I will brief this morning.

Thank you for the opportunity of appearing before you today to discuss the FTC's role in the regulation of the cosmetic advertising.

As you know, the Federal Trade Commission polices unfair and deceptive acts or practices for a broad range of products. Both the FTC and the FDA have overlapping jurisdiction over the advertising and labeling of food, drugs, and cosmetics and devices.

Since 1954, the two agencies have operated under a liaison agreement which allocates the responsibilities between us. The agreement has resulted in a long-standing degree of cooperation between the agencies, each having primary jurisdiction over the areas in which it has developed expertise.

The agreement basically provides that, except for prescription drug advertising, the Federal Trade Commission has primary responsibility to regulate the advertising of food, drugs, cosmetics, and devices, and the FDA has primary responsibility for preventing the misbranding or mislabeling of food, drugs, and cosmetics.

Under the agreement, the FTC and the FDA will avoid initiating separate proceedings against the same party except when such action is in the public interest.

We monitor national advertising in both print and broadcast media on a regular basis. In addition to our monitoring, both competitor and consumer complaints can be an important source of information concerning potentially deceptive, unfair or unsubstantiated claims, and, finally, referrals from other Government agencies, such as the Food and Drug Administration, and State and local consumer protection agencies often are an important source of leads.

On deception, in deciding whether a particular ad contains a deceptive claim, the Commission concerns itself with how consumers are likely to perceive the claims made in the ad.

The principal case selection criteria we employ is the extent of consumer injury caused by the advertising. Traditionally, cosmetic advertising has relied heavily upon a combination of puffery and subjective claims about beauty and, for the most part, our program has not focused on such claims.

Instead, we have concentrated our efforts on advertisements for products that include health or safety claims or that otherwise present a significant risk of injury when used. Examples of these types of claims are provided in my written testimony. I will give you a brief sample here.

They include Commission actions to require warnings on hair straightener advertising, and Commission actions to prevent deceptive safety claims for artificial sun tanning equipment, and to require affirmative disclosures that tanning devices carry FDA labels warning of the risk of skin cancer and eye injury whenever the ads make safety claims.

While focusing on health and safety claims, the Commission also brings cases against claims posing primarily the risk of economic injury. Thus, for example, the Commission has brought actions against marketers of cosmetic hair products which falsely claim they prevent or cure baldness, and actions against individuals allegedly offering painless laser face lifts at a cost of $750 to $1,500 apiece, which the Commission charged were ineffective.

We also conducted investigations of antiaging claims made by some cosmetic manufacturers. However, our activity on those investigation took a back seat with the FDA's action that you heard about this morning, that was taken on an industry-wide basis last year.

We are continuing, however, to monitor the advertising in that area, and we will initiate followup investigations where necessary.

Our investigations of cosmetics are normally carried out under our advertising substantiation program. Under this program, it is an unfair and deceptive practice for an advertiser to make an objective product claim unless the advertiser has a reasonable basis for believing that the claim is true at the time it is made.

Investigations of a company's advertising substantiation normally begins with a letter to the company in which the staff sets out its concerns and asks for substantiations about the claims that concern the staff.

If the company refuses to comply with those requests, the staff may request authorization from the Commission to issue a compulsory process requiring production of such material.

On the sharing of information about which you were interested, Mr. Chairman, the proprietary data supporting the company's claims that is obtained in Commission investigations can be disclosed only to Federal Trade Commission employees.

However, FDA staff members and outside experts may be retained by the Commission as Commission consultants, but are required to sign nondisclosure affidavits before they can be given this information to review.

Furthermore, the Commission may provide confidential information to other Federal agencies provided that information is maintained in confidence and used only for official law enforcement purposes.

I hope that has given you a useful and quick summary of our approach to cosmetic claims, and I appreciate the opportunity to answer any questions that the committee may have.

[Mr. MacLeod's statement may be found in the appendix.]

Chairman WYDEN. Thank you both. You have been very cooperative.

Let me see, first, if I can look at some of the worker health issues as they came up, Mr. Adkins, at our previous hearing. What we heard, frankly, from the folks who work in the beauty industry really was of substantial concern.

It is my understanding that very often the cosmetics that they use are in bottles that are unlabeled. They are clear bottles and there are not specific indications on the bottle exactly what is in it, is that correct?

Mr. ADKINS. I do not have knowledge of that. With the expansion of the Hazard Communication Standard into all segments of industry, those materials would be required to be labeled, with the exception as they might apply to consumer products.

We have been held back on the application of the standard to consumer products because of our need to assess its information collection burden.

Chairman WYDEN. But that is not labeling. Maybe you can help us with that, Ms. Silk.

We were told, have been told in a number of instances, that very often folks in the beauty industry, when they reach for one of these bottles, there is no explanation of what is in it at present, is that correct?

Mr. ADKINS. There is a requirement for hazard warning on that material, and the material safety data sheet should be submitted with that.

Chairman WYDEN. I am talking about the bottle, Mr. Adkins. What I want to know, first of all, is what we were told correct, where folks in the beauty business today, when they are giving someone a shampoo or something of that nature and reach over for that bottle, is that bottle unlabeled today?

Ms. SILK. It should not be. Sir, I think we need to make clear that these requirements for hazard communication only went into effect very recently. They only became fully effective on August 1. So, when you're talking about things that occurred several years ago, there would not have been a requirement at that time.

Chairman WYDEN. Will these new requirements ensure that there is labeling on the bottle?

Mr. ADKINS. Under today's rule, it would be a violation of the Occupational Safety and Health Act to have an unlabeled container.

Chairman WYDEN. What would be on the bottle? Would there be a requirement that the ingredients be on the bottle?

Ms. SILK. No; there is no such requirement—under Hazard Communication. We have a three-pronged approach, and we believe all these things are interdependent on each other.

A label, we believe, is intended to give you a quick synopsis of what the hazards are. There is a lot of evidence to indicate that the more information there is on a label, the less likely it is anybody is going to read it or understand it.

So, under our approach, we have the hazards and a link on that label, some identity that will get you to the material safety data sheet, which is required to be available to you when you are in the workplace.

That MSDS will list all the ingredients. It will also list the precautionary measures and other information that you need to protect yourself.

In addition to that, the workers have to be trained so they know how to use that information and know how to access it. We believe that what makes it all effective, is really understanding the information.

Chairman WYDEN. I think I understand what is going on, that there will be a warning, but under your rule, labeling of the ingredients still is not required.

Ms. SILK. No; the label would say—it could say hair spray number 55, flammable, causes lung damage, and then you would look at the data sheet for hair spray number 55 and it would tell you what the hazardous ingredients are.

Chairman WYDEN. OK.

Mr. ADKINS. We need to reemphasize, too, this comes about with the expansion of the Hazard Communication Standard into all segments of industry. As initially published, it did not include those segments.

Chairman WYDEN. We were also told that very often, these establishments—again those that might not be up to par in recognizing that the vast majority have worked hard on safety issues as most businesses—but that there is a substantial minority of these places that are poorly ventilated and that do not have particularly safe working conditions from the standpoint of ventilation, light, and exposure. Is that correct, Mr. Adkins?

Mr. ADKINS. I cannot say that it is correct or incorrect, sir. I have been in places that do not have ventilation for sure.

Chairman WYDEN. What has your agency found? What do inspections show? Is there a substantial number that are poorly ventilated and have caused health problems for that reason specifically?

Mr. ADKINS. Our inspection activity in the past has been toward high hazard industries, and beauty salons have not been in the high hazard list, and we have not had a lot of inspection activity. We have had some, but it does not indicate that that is an overall general problem.

OSHA allocates its inspection resources as much as possible to high-hazard workplaces. The incidence of serious work-related injuries is, we believe, the best indicator of the extent of potential safety hazards in an industry or in an establishment. By serious injuries, we mean those that result in time lost from work, or lost workday injuries.

On this basis, several injury groups, principally in the manufacturing and construction sectors, have inspection priority and appear to warrant greater attention from OSHA than barber and beauty shops. Among these are high-hazard manufacturing workplaces such as meatpacking plants, steel mills, foundries, paper mills, shipbuilding and repair facilities, and wood products manufacturing plants. Some manufacturing workplaces have annual lost workday injury incidence rates [LWDI] as high as 17.2 per 100 full-time workers, according to 1986 figures published by the Bureau of Labor Statistics, compared to a rate of 3.6 for the private sector as a whole. The construction industry rate also is higher than average, with a 1986 LWDI of 6.9.

By contrast, the 1986 LWDI rates for beauty shops is 0.5 lost workday injuries per 100 full-time workers—about one-seventh of the average rate for all U.S. industries, and many times lower than the rates for construction and high-hazard manufacturing where OSHA focuses its discretionary inspection efforts. Although BLS does not publish a LWDI for barber shops, we believe it also would be far lower than average.

Chairman WYDEN. All right. We will stipulate then that you really do not know whether there are many that are poorly ventilated because you have not been out there doing these inspections.

How many inspectors are employed by OSHA, Mr. Adkins, to follow up when you have indications of a problem case? How many people do you have budgeted to try to follow up not on everything but on the problem cases?

Mr. ADKINS. We have approximately 1,200 compliance officers in the Federal program. In the total program, we have a little over 2,000 compliance officers, State and Federal.

Any of those compliance officers would be available to investigate a complaint if we received a complaint from an employer about a work site. Any of them conduct inspections in work sites.

We do not have a body of people specifically for a particular industry.

Chairman WYDEN. So, you really do not have any specific number? The number is zero for inspections specifically when there is a problem in the beauty shop or barber shop?

Mr. ADKINS. The number is over 2,000, sir.

Chairman WYDEN. But not specifically to do beauty and barber shops?

Mr. ADKINS. They are specifically assigned to do safety and health inspections in the work site.

Chairman WYDEN. How many did inspections on the problem cases in beauty and barber shops last year? Of that 2,000, how many actually did an inspection last year?

Mr. ADKINS. I am not sure I have last year's data. I have some data for several years, and there was something like, I believe I recall, 88 inspections or something like that over the last several years in beauty salons.

Chairman WYDEN. What year was that?

Mr. ADKINS. That was over the last several years.

Chairman WYDEN. So, over the last several years——

Mr. ADKINS. In the last several years, there have been 88 total inspections in beauty shops.

Chairman WYDEN. That averages about eight inspections a year. Let me ask you about some of the health concerns that the workers have raised to the subcommittee.

You consider there to be significant health problems for workers as a result of exposure to formaldehyde in beauty and barber shops?

Mr. ADKINS. In barber shops? I am not aware of specific hazards in barber shops of formaldehyde. We do regulate formaldehyde. We think it is a significant hazard. We promulgated a new rule in the past year on the exposure to formaldehyde to anyone in any workplace, not just in barber shops.

Chairman WYDEN. But you have not looked whether formaldehyde is a health problem for workers in beauty and barber shops specifically?

Mr. ADKINS. Typically, when OSHA develops a regulation, we do a regulation to protect all workers, not a regulation for a specific work environment.

Chairman WYDEN. Have you looked specifically——

Mr. ADKINS. Not in barber shops, no, sir, for formaldehyde.

Chairman WYDEN. How about beauty salons?

Mr. ADKINS. Not to my knowledge, no.

Chairman WYDEN. Have you looked at the potential health exposures for workers in beauty and barber shops of methylene chloride? That is a neurotoxin and possible carcinogen.

Mr. ADKINS. Yes; and we are doing rulemaking on methylene chloride at the present time, but not specifically for barber and beauty shops. Again, we do not do things for specific industries. We do regulations for all employees, to cover all employees.

Chairman WYDEN. How about with respect to ethyl methacrolate? That is an allergen and what has been described again as a suspected neurotoxin. Have you all looked at potential health exposures to workers in beauty and barber shops to that chemical?

Mr. ADKINS. No; we have not.

Chairman WYDEN. Do you intend——

Mr. ADKINS. We have——

Chairman WYDEN. Do you intend to? Is that something you think should be done and you have not gotten around to it or?

Mr. ADKINS. Mr. Chairman, when we look at a chemical substance, we do an overall look at that chemical substance, and I am certain that we look at potential exposures in every industry. If you are asking have we gone in and specifically sampled in this segment, no, but we looked at the toxic effects on the inspection records that we have now and at the injury and illness records that we go by for targeting. We look at that kind of information to determine where the exposures are and what the potential exposures are and then we regulate accordingly.

But the regulation is developed on the toxic effect of a chemical, not to the employee, not to a specific employee in a specific industry, but to any employee in any industry.

Chairman WYDEN. No; I understand your desire to look at the workplace as a whole. My concern is whether anybody is following up specifically on these concerns that workers are bringing to us about beauty and barber shops, and I gather from your testimony that there has been no——

Mr. ADKINS. It is not a priority area for scheduled inspections, but if we have complaints from workers in this area, we would investigate those complaints.

Chairman WYDEN. Have you had complaints in the last year from workers in this field?

Mr. ADKINS. Based on these numbers of 1988 and the last 10 years, some of those probably were complaints, but that is not many.

Chairman WYDEN. So——

Mr. ADKINS. That is what would have been what put us in a beauty shop, a complaint.

Chairman WYDEN. You are not initiating any kind of followup yourself? This is when they call you about eight times a year, you all go out there and take a look?

Mr. ADKINS. We are prohibited by an appropriations amendment from Congress from scheduling safety inspections in work sites of 10 or fewer employees, and where they are not above the national average on injury incidence rates. Beauty shops are currently not above the national average on injury incidence rates. So, we cannot expend money going in those places where there are 10 or fewer employees unless we get some type of a complaint.

Chairman WYDEN. I am going to forward some to you because we had a number of workers come to our last hearing and they and unions, the United Food and Commercial Workers specifically, are very unhappy about the lack of protections, and they say, as I have said, that nobody is talking about getting rid of these products or prohibiting anybody from using them in beauty shops.

What we are talking about is basic kinds of protections. That the bottle be labeled so that people know what is in the bottle, that there be followup on problem cases when there is actually a problem, and——

Mr. ADKINS. I would submit to you today that in any beauty salon, if there is a product that an employee is using that does not have a label, they are in violation of the Occupational Safety and Health Act.

Chairman WYDEN. We are not talking about the warning label. We are talking about ingredients. The question of employees being able to——

Mr. ADKINS. Our law does not require the ingredients to be put on the label.

Chairman WYDEN. I understand that, I understand that.

Let me ask one additional question, then we are going to have to break for a vote.

You said the States are maintaining programs in this area. Are you satisfied that States have been following up when there is a problem in a beauty or barber shop?

Mr. ADKINS. States have to respond in the same way that the Federal compliance officers respond when they receive complaints. They are governed by the same restrictions that the Federal people are governed by, and State plans have to be at least as effective as the Federal plans, and they are monitored to be sure that they are.

Chairman WYDEN. Have you done an assessment of these State plans to follow up on problems in beauty and barber shops?

Mr. ADKINS. No; not on that specific industry.

Chairman WYDEN. How do you know the programs are working?

Mr. ADKINS. We do an assessment on how they follow up on complaints, and today, the only way that anyone could get in it would be in response to a complaint. We could not schedule inspections in a beauty or barber shop. Those are not program inspections. They are not high hazard industries, and we cannot program inspections in those work places.

Chairman WYDEN. Why do you not give us, for the record, your appraisal of the State programs? I noted that you felt that that was an important tool, and I would like to see your evaluation of how those programs are working.

Mr. ADKINS. The Occupational Safety and Health Act of 1970 [OSHA] encourages States to develop and operate their own occupational safety and health programs, or plans, under Federal guidance and monitoring. To foster that partnership, the act authorizes OSHA to provide up to 50 percent of a State plan's operating costs. There are currently 25 States, or jurisdictions, operating occupational safety and health programs approved by OSHA, 22 of these programs cover both private and public sector employees, and 3 plans cover public employees only. Approximately 35 percent of the Nation's private sector workforce is covered by State OSHA programs.

Under section 18(f) of the OSHA Act, OSHA is required to evaluate the manner in which the States administer their programs. In general, State performance is expected to be at least as effective as the Federal OSHA program. The agency's State plan monitoring and evaluation system compares State performance with Federal performance by measuring activity within 11 major program areas, including standards, enforcement, consultation, and variances. Most of the data necessary to evaluate State performance are obtained through a computer-based system. If a State's performance differs significantly from the criteria established by OSHA, or if OSHA believes further inquiry is warranted, in-depth analyses are performed. Such analyses may include onsite review of State files and inspection activity to determine the reason for the apparent divergence in State performance. Periodically, OSHA provides State plan administrators with evaluation reports that summarize the results of Federal monitoring.

At this time, none of the State plans are experiencing significant problems in administering the program. All States are providing protection that is at least as effective as the Federal program. This does not mean that every State plan is identical to Federal OSHA.

There is little inspection activity in beauty parlors and barber shops by Federal OSHA. The same is true for the States. The agency's overall evaluation of State programs addresses their activities in all the workplaces covered by their programs, including those in the cosmetics industry. OSHA, however, does not specifically evaluate the performance of the State plans vis-a-vis those workplaces.

Chairman WYDEN. One last question, if I might. Considering the conditions of the typical beauty parlor and the compounded amounts of the chemicals being used each day by a cosmetologist, do you think that that produces an environment for the workers that can be a public health concern?

Mr. ADKINS. That the chemicals——

Chairman WYDEN. Yes; they are in those places. They are using the chemicals day in and day out, often in a place——

Mr. ADKINS. I would say there is a potential for exposure to toxic chemicals, yes.

Chairman WYDEN. We will break then and let us say we will reconvene in about 15 minutes.

[Recess.]

Chairman WYDEN. The subcommittee will come to order.

I want to thank our witnesses for their patience. Today, we have a lot of votes up, and I appreciate your indulgence.

Mr. MacLeod, I want to make sure I understand exactly your relationship with the FDA.

When you find evidence of a misleading claim, you are barred from giving that information to the FDA?

Mr. MACLEOD. No; we are not barred, but we have to go through a procedure whereby the FDA can confirm to us that it will use it for law enforcement purposes and keep it confidential. So, we can share that kind of information.

Chairman WYDEN. All right, and what kind of procedure is this and how often is it used?

Mr. MACLEOD. It is used reasonably often. I do not have a count of the instances because it is a reasonably routine procedure, and it is simply a letter from another agency, like the FDA, to us certifying that the material will be kept confidential and will be used for law enforcement purposes.

That is sufficient for us to release the information to another law enforcement agency.

Chairman WYDEN. But do you contact them and ask them to get you this letter, otherwise how would they know about it? You have the information. You call them up and say you can have this information if you submit a letter?

Mr. MACLEOD. It works both ways. If we find something that we believe is within their jurisdiction, it is something in which they have a law enforcement interest, you can be sure we will be on the phone very quickly.

Chairman WYDEN. What I am interested in is information that would relate to on-going safety considerations, where there is a misleading claim.

Mr. MACLEOD. We have brought cases dealing with cosmetics that involve safety claims ourselves, and there are times, for example, when there is a safety claim in the advertising that we think we can address and that resolves the issue. Then we will go ahead and bring the case ourselves.

If it is a case, however, that seems to go beyond that jurisdiction of the Federal Trade Commission, and we think that there is something the FDA can also do, we will contact the FDA.

In addition, even when we are proceeding on our own, we will often be in contact with the FDA to make sure that they understand what we are doing and we often also consult with the FDA because they are a primary source of our experts and our witnesses.

Chairman WYDEN. I would like a list of the instances where this is actually done. Could you furnish that to me for, say, the last 2 years, where you have been in touch with the FDA or they have been in touch with you, as you say the relationship works?

What we want to see is exactly what kind of a regulatory framework there is and to do that, I think it would be helpful to have some concrete cases. Can you furnish that to us?

Mr. MACLEOD. I will try to give you some examples, but I suspect that with the number of phone calls and contacts that have taken place over the past couple of years, someone might not remember——

Chairman WYDEN. Why do you not give me some of the major instances where the two of you have shared data and teamed up to help us address some of these safety issues?

Mr. MACLEOD. Are you speaking safety issues with respect to the cosmetics?

Chairman WYDEN. Yes; safety issues with respect to cosmetics. All right?

Mr. MACLEOD. Yes; we will provide for the record what we can put together.

Chairman WYDEN. All right. Now, it is our understanding that the FTC is now conducting a preliminary nonpublic inquiry on an antiaging cream produced by a U.S. manufacturer. Is this the only inquiry involving a cosmetic product at this point?

Mr. MACLEOD. No; it is not. We have a number of inquiries in various stages. However, if you mean as far as antiaging is concerned, what we have done in that area has been to take a back seat to the FDA action because they have moved on an industry-wide basis, and if FDA's action resolves all the problems, then that is the kind of thing that our liaison agreement contemplates—that we would not spend duplicate resources pursuing the same cases.

Chairman **WYDEN**. How many inquiries have there been in the area of cosmetic products?

Mr. **MACLEOD**. How many inquiries have there been?

Chairman **WYDEN**. Yes; our staff has been told about 15 investigations involving cosmetic products.

Mr. **MACLEOD**. That is a good number for recent years. However, when you ask have there been—I would need to have a timeframe.

Chairman **WYDEN**. Let us say the last 5 years. Is 15 the number over the last 5 years or 2 years?

Mr. **MACLEOD**. Fifteen over the last 2 years—over the last 5 years. I believe that is a good——

Mr. **PEELER**. I believe that number is since 1985 for cosmetic claims.

Chairman **WYDEN**. So, there have been 15 investigations of cosmetic claims over the last 3 years?

Mr. **MACLEOD**. That is correct.

Chairman **WYDEN**. Not necessarily antiaging, just cosmetic claims generally?

Mr. **MACLEOD**. That is correct. Not necessarily safety either. Some could be efficacy claims.

Chairman **WYDEN**. During this period of investigation, particularly if you find grounds to believe that there is a real problem, not simply a de minimis kind of problem, is the manufacturer restrained from peddling the product?

Mr. **MACLEOD**. We have the power, if we believe that there is a sufficient immediate danger to the public, to seek an injunction in Federal court. But as a typical matter, the answer is no. We go through administrative proceedings at the Federal Trade Commission, which result in a cease and desist order which then prevents the marketing or the advertising practice we object to.

Chairman **WYDEN**. The subcommittee noted that the manufacturer's submission of data with respect to claims substantiation is very technical.

Does your agency have the expertise to understand these claims and, in effect, make a determination whether the product lives up to its claim?

Mr. **MACLEOD**. We seek the expertise. We are primarily an agency of lawyers, but we often employ consultants. We use contractors, and I might add, one of our principal sources of experts is the other Government agencies. FDA is a prime example.

Chairman **WYDEN**. Do you all have the expertise in order to determine whether antiaging products can live up to their claims?

Mr. **MACLEOD**. That is the kind of case in which we would employ experts. We do not have in-house scientists, physicians, or Ph.D.'s.

Chairman **WYDEN**. Are you employing somebody on that right now?

Mr. **MACLEOD**. We have employed consultants in the past, and we do have them available, yes. As I say, the antiaging issue is a category where the FDA is moving across a broad front of the industry, and we are seeing how that move is working.

Chairman WYDEN. So, you feel you do not need to move on this particularly right now, given what FDA is doing?

Mr. MACLEOD. We are monitoring the industry. I would not be willing to concede that there is nothing for us to do there. If I see a problem out there, I will move. Right now, however, I do not want to duplicate the effort the FDA is undertaking.

Chairman WYDEN. Your testimony also stated that most of the cosmetic advertising cases that the FTC has brought in the past have involved products or claims for which there were safety concerns. Was it not your finding that these products contained chemicals which were hazardous?

Mr. MACLEOD. In some cases, that is correct, yes.

Chairman WYDEN. Which cases were those?

Mr. MACLEOD. Well, for example, hair straightener cases that contain caustic chemicals that might cause irritation to the skin. Those are the allegations that are made in the complaints, and that is the kind of case that results in an information disclosure order from the Commission cautioning consumers to that property of the product.

Chairman WYDEN. Are those products generally still on the market then?

Mr. MACLEOD. Products with those kinds of chemicals are generally on the market with a disclosure that cautions the consumer about their use.

Chairman WYDEN. Why do you not give us a list for the record of those products as well? The products where you found grounds for safety concern and actions that were taken with respect to warnings and indications that care should be taken with the use of those products.

Mr. MACLEOD. Be glad to, Mr. Chairman.

Chairman WYDEN. Unless you all would like to add anything further, we will excuse you at this time. Thank you for your patience.

Mr. ADKINS. Thank you.

Chairman WYDEN. Dr. Robert Elder, director of Cosmetic Ingredient Review Board, Washington, DC. Doctor, if you will come forward.

Doctor, we welcome you to this subcommittee. You have been here, I note, throughout the morning. Do you have any objection to being sworn?

Dr. ELDER. No, sir.

Chairman WYDEN. Please rise and raise your right hand.

[Witness sworn.]

Chairman WYDEN. Doctor, do you desire to have counsel with you during your appearance today?

Dr. ELDER. No, sir. I know I sit somewhat alone, but I am from Oregon State.

Chairman WYDEN. That puts a totally different light on it. Very, very good, and we welcome you.

We will make your prepared remarks part of the record in their entirety, and if you could summarize some of your principal concerns in your oral presentation, we have gone way late in this hearing, and in the interests of time, that would be helpful.

## TESTIMONY OF DR. ROBERT ELDER, DIRECTOR AND SCIENTIFIC COORDINATOR, COSMETIC INGREDIENT REVIEW BOARD, WASHINGTON, DC

Dr. ELDER. Thank you, Mr. Chairman.

Mr. Chairman, members of the committee, my name is Robert Elder. I have been the director and scientific coordinator for over 9 of the 11 years the Cosmetic Ingredient Review has been in existence.

Prior to this, I was an assistant surgeon general in the U.S. Public Health Service and a Deputy Associate Commissioner for Science in the Food and Drug Administration.

With your permission, I will summarize these comments and submit the full text for the record.

Dr. William Berndt, the chairman of the CIR panel regrets that his responsibilities as the vice chancellor of the University of Nebraska Medical Center prevented him from being here. He has written a letter to the committee that I would like to have inserted into the record.

Chairman WYDEN. Without objection, that will be ordered at this time.

[Letter referred to above may be found in the appendix.]

Dr. ELDER. The Cosmetic Ingredient Review was established as a cosmetic industry self-regulatory program in 1976 by the Cosmetic, Toiletry and Fragrance Association. The program's sole mission is to evaluate the ingredients, safety of ingredients used in cosmetic products.

The CIR program was designed to bring together for public review and evaluation all of the worldwide data, both published and unpublished, on cosmetic ingredient safety.

The CIR Program and procedures are modeled after the Food and Drug Administration's review of ingredients used in nonprescription drugs. The written procedures, which I would like to submit for the record, describe the detailed requirements that must be followed in evaluating the safety of cosmetic ingredients.

The program has four important fundamental characteristics. The review must be conducted in an open public manner where any person may participate. All data considered by CIR and the expert panel, including test methods, administrative records, must be publicly available for review by any interested person.

All decisions relating to the safety of cosmetic ingredients are made by an expert panel of seven independent academic scientists. The fourth, the CIR Program and its staff, consultants, scientists, are funded by but separated from the cosmetic industry.

All reports issued by CIR are released to the public without prior CTFA or industry review. Proof of the safety of a cosmetic ingredient must be documented through scientific evidence. A long history of safe use or the lack of adverse information is not sufficient to demonstrate proof of safety.

The CIR procedures established two separate committees. The first, a steering committee that I report to, provides policy advice and guidance to the overall CIR Program. It has two members from CTFA, one member from industry, an academic toxicologist selected by the Society of Toxicology, an academic dermatologist selected by the Academy of Dermatology. This group appoints the expert panel who are appointed from publicly-nominated individuals.

Each member of the CIR expert panel must satisfy the same strict conflict of interest requirements that are imposed upon special Government employees who serve on advisory committees under Federal law. They may not consult with or have any financial interest in any cosmetic manufacturer or supplier.

In addition to the seven scientific experts, the expert panel includes a consumer liaison, selected by the Consumer Federation of America, an industry liaison, selected by CTFA, and an FDA contact person, selected by FDA.

The expert panel is supported by a full-time staff of eight and has an overall budget which does not include funding for testing of $750,000 a year.

The expert panel evaluates the safety of each ingredient according to a priority list which establishes a time sequence for ingredient review. The eight factors used to calculate an ingredient's priority for review are as follows: Biological activity, which I would like to note for the record, is a much wider term than toxicological data. It means the ability of the ingredient to interact with biological systems.

Frequency of use. Estimate of skin penetration. Area of skin application. Frequency of application. Frequency of consumer complaints. Use by sensitive subgroups in the population and the concentration of use.

The CIR staff priority calculations and the preliminary priority lists of ingredients are first reviewed by the CIR steering committee. In the steering committee's review of the 1977, 1980, and 1984 priority list, they made no changes in the order of any ingredient on the list.

After the steering committee's review, the proposed list is made available for a 90-day public comment period. During this time period, any person may make recommendations or give opinions. To date, requests for changes in the order of priority have been made only for an increased weighting for biological activity.

In the 1984 priority list, comments were received from the Food and Drug Administration, from a prominent dermatologist, and from industry. All recommendations by the Food and Drug Administration were accepted. All recommendations by the dermatologist were accepted. Some of the comments received from industry were not.

In the 1984 priority list, which involved prioritizing 331 ingredients into a final list of 233 that we call the current list, there are 71 ingredients deferred because they are OTC ingredients or direct food additives. There are 27 ingredients which are inorganic and were deferred by the panel.

The panel concurred with the comments as noted with the dermatologist and with the FDA and the changes were accepted.

Many cosmetic ingredients, which are in use today, are already approved as a food and drug ingredient. As I noted, the panel deferred OTC ingredients. There are other areas, such as food additives and ingredients approved in new drug applications, which have a low priority for review.

These ingredients are deferred. They are nonexempt. Eventually, they will be subject to CIR review. All ingredients that are subject to a final regulation by the Food and Drug Administration are exempt.

I would like to call the committee's attention particularly to the problem involved in establishing a list for review. The CTFA ingredient dictionary lists approximately 5,000 nonfragrant ingredients that are offered for use by the cosmetic industry.

It is estimated that only 2,300 of these nonfragrance ingredients are actually used in cosmetics at any one time. Data from the FDA voluntary cosmetic reporting program indicates that approximately 700 of these 2,300 ingredients have been reported to be used in 20 or more cosmetic formulations.

The 700 ingredients whose reported frequency of use is greater than 20 are the ingredients that have thus far been prioritized for CIR review. Although we have prioritized all those ingredients used in 20 or more formulations, in going through this process, we have actually considered a much larger number of ingredients.

We considered all ingredients in 10 or more formulations when we established the 1984 priority list to make sure that an important chemical was not missed.

Even after the priority list is established, the expert panel reevaluates the priority list every 12 to 18 months. In 1987, FDA provided to the expert panel a list of all ingredients voluntarily reported to them that were used in any cosmetic formulation. This was reviewed by the panel.

So, we have cast and continue to cast a large net to obtain the ingredients of use in the cosmetic formulations of today. It is important to note that ⅓ of the 700 ingredients which are in our target population are already regulated by FDA for use in foods, drugs or as color additives.

After an ingredient has been prioritized for review, the staff prepares a scientific literature review which contains all of the available published safety information. This scientific literature review is released for a 90-day public comment period with a request to industry and all other interested persons to provide any unpublished safety information they may have in their files, as well as, any comments or suggestions to improve the report.

After the 90-day comment period, the unpublished data is incorporated into the report and submitted to the expert panel for review. After a review of all of the information in the scientific literature review, published and unpublished, the expert panel makes its determination on safety.

The CIR procedures specifically require that the panel make one of three decisions. Safe for use, with or without limitations; unsafe for use; or insufficient data to determine safety.

If an ingredient is judged to be either safe or unsafe, a tentative final report is released for a 90-day public comment period. After the public comment is received, a final report is issued. If an insufficient data determination is made, industry is notified that certain specific test data must be supplied. If no one offers to support the request to testing, CIR proceeds to issue a final report determining that there are insufficient data.

Any person may review or comment on the CIR documents, agreeing or disagreeing with them. The CIR expert panel must respond in its final report to every comment. At any meeting of the CIR expert panel, any individual may request to address the panel on any ingredient under review. The expert panel chairman, Dr. William Berndt, and his predecessor, Dr. Karl Beyer, have always permitted any individual in attendance at its meetings to provide comments or ask questions on the topic or report under review. Thus, the program is open to full public scrutiny and must be, and is, responsive to all public comment.

After a final report is issued, the report is then submitted to the Journal of the American College of Toxicology for their own editorial review and acceptance prior to publication in a special issue of that journal.

Fourteen journal issues containing CIR reports are now available. The 15th issue has been reviewed and accepted by the editor for publication.

The data ordinarily considered in a CIR report includes a detailed chemical description of the ingredient, including specifications and impurities, the use of the ingredient in cosmetic products, including the concentration of use in each and every product, animal safety data, which may include subchronic/chronic toxicity, eye irritation, skin irritation, sensitization, immunogenicity testing, and human safety test data, which may include skin irritation, sensitivity, and photoallergenicity.

In determining the scientific test data needed to substantiate the safety of a cosmetic ingredient, the CIR expert panel applies generally accepted principles of toxicological evaluation. Rather than use an arbitrary list of standard tests, the panel determines the test data needed for an ingredient by reviewing all aspects of the substance.

In many instances, all of the data needed for the expert panel already exists. In some instances, further test data are required. Experience with the CIR review has shown that the careful and methodical scientific review given by the expert panel and the documentation of the specific need for any additional testing requested by the expert panel normally prompts the industry to do any testing required to prove safety.

The full public discussion of the scientific rationale for requesting further testing rather than a boiler plate checklist approach places the burden of publicly-defining need to test on the expert panel.

As of August 1, 1988, the expert panel has issued a 112 final reports covering 277 ingredients. In the course of completing these reports, the expert panel issued 22 insufficient data announcements. Thirteen of these insufficient data announcements resulted in a positive response from industry to supply the appropriate data required to make the safety decision. Nine did not.

Of the 277 ingredients reviewed, the expert panel concluded that 237 are safe for use in cosmetic products in their present conditions of use. Use limitations have been included in conclusions for 30 ingredients. One report the expert panel found the ingredient, p-hydroxy-anisole, unsafe for use in cosmetic products under any conditions.

There are currently 32 reports on 49 ingredients at various stages of development and review. I would like to note that in this latter group under review, there is another ingredient that the panel has declared unsafe. It is at the final stages of public comment.

Mr. Chairman, CIR is always open to new information. If this committee has any information which indicates that cosmetic ingredients should be added to our priority list, we would like to have that information. CIR will take this information, complete the necessary staff analysis, present it to the expert panel for their consideration at the scheduled January 1989 meeting.

The expert panel's decision and rationale for acceptance or rejection of a requested accelerated view or the addition of new ingredients to the priority list could be sent back to this committee by mid-January.

In accordance with this morning's testimony and the 884 ingredients of interest to this committee perhaps it might be appropriate to apply the CIR procedure for establishing priority on this group. I am not certain we could get them past the expert panel that fast, but I am certain we can report back to this committee in January of how those 884 ingredients would have stacked up had they gone through the CIR priority procedures.

[Dr. Elder's statement may be found in the appendix.]

Chairman **Wyden**. I note particularly your last comment. You would feel that is important for you to go through those 884 cases and try and identify the priorities and make an assessment of them?

Dr. **Elder**. Yes; Mr. Chairman, when I took this job, one of the real concerns was the priority list. I discussed the criteria with the staff of the National Academy of Science, for my predecessors followed very closely their recommendations on how to prioritize. That can be found in the National Research Council's 1982 Report to the National Toxicology Program.

One suggestion we did incorporate into priority setting procedure was received from FDA. That is the estimate of penetration factor that I previously mentioned as one of the major factors we use. That was added in.

Chairman **Wyden**. What was it you said you could get done by January? I was not clear on that.

Dr. **Elder**. I committed CIR to look at the 884 ingredients you have. We would apply the CIR procedures for establishing priority and see how they would rank if you had submitted that list independently as a comment to CIR.

Chairman **Wyden**. That would be very helpful and useful.

Let me see if I can ask a couple of straightforward questions and then we will get in to some more of the technical issues. Does your organization actually test ingredients in cosmetics?

Dr. **Elder**. No, sir. That is the key to the insufficient data report which is a public document in which industry is told that testing must be done or the panel cannot reach a conclusion on safety. Industry has to provide the testing.

Chairman **Wyden**. OK, do you verify the company's test data?

Dr. **Elder**. I do not see company names. In my testimony, I mentioned that there is an industry liaison on the panel. He is informed in a very formal manner. The records of those requests are available. He contacts the industry.

It may be one or more manufacturers involved in supplying needed data. I am not aware of how many people support it, only if it is done.

Chairman WYDEN. Doctor, are not those two pretty significant limitations? I have a number of other areas I want to go into, but it strikes me that if you all cannot actually test ingredients and you cannot verify company test data or how long the test was done for or how well the test was done. Are those not pretty serious limitations?

Dr. ELDER. In summarizing my response, I left out some key points, such as, all data tests sent to CIR must have the test methods attached to it. We accept no data without test methods. You cannot correlate the data if this is not available.

Chairman WYDEN. But test data is not given to FDA. We heard Commissioner Young this morning say that he does not have the legal power to require the test data be given to them, that he has asked in what was described as many instances and could not get it.

Dr. ELDER. Yes; CIR is a voluntary regulatory program. We have asked for data 30 times. We received it for 21 of the 30 requests. Nine times we did not get data. This means that the safety of the ingredient we reviewed has not been documented. I do not have that problem that FDA has.

Chairman WYDEN. Let me ask you a little bit about your work then.

Now, it is my understanding that 300 chemicals or thereabouts have been reviewed or are undergoing review, is that correct?

Dr. ELDER. Yes, sir.

Chairman WYDEN. Can you explain how those were prioritized and how it happened you chose those 300?

Dr. ELDER. Yes, sir. Under the voluntary program that FDA conducts, manufacturers report the ingredients that are being used, as well as the numbers of formulations in which they are used.

FDA provides us a list of the most frequently used cosmetic ingredients. For example, a recent list I looked at a couple of years ago, one ingredient was used in over 7,000 formulations. Other ingredients are used in only one.

The big problem we have is that a lot of the ingredients in the CTFA dictionary are offered for sale but are not used. The reported frequency of use is one of the main criteria we use in establishing the priority list. I think it contributes about 22 percent of the total. It provides an estimate of exposure. The frequency of application, is also an estimate of exposure. We try to have exposure criteria in our priority setting, that estimates how people are being exposed to the most frequently used ingredients.

Chairman WYDEN. I understood that you all used the frequency standard as your principal way of dealing with it.

It is my understanding, also, that the European Economic Commission, for example, approves ingredients used by their manufacturers in a way so you target on the chemicals that are known or reported to be toxic substances.

Is there a way in your system to make a priority of those substances that are known or reported to be toxic? My sense is that you go on the basis of frequency.

I think that is certainly relevant and I have no quarrel with going that route, but I am concerned that there does not seem to be a system that really goes after toxic substances, as is done in Europe, because the things that are toxic ought to be at the top of the priority list.

Dr. ELDER. I am familiar with the EEC system. We have an exchange program through an organization called COLIPA. The EEC system is what in the health field we call an active or hit list. That is a very difficult procedure they use. When they put all of the preservatives used in cosmetics on one list to be reviewed, the manufacturer does not know which way to turn until the review was completed.

We have reviewed all of the EEC lists. I know of no ingredient that is prohibited on the EEC list that is awaiting review by the CIR. The ingredient I previously mentioned was declared unsafe by CIR, can be used in EEC.

We also track the Japanese safety evaluations. They list ingredients that can be used rather than the ones that cannot be used.

Chairman WYDEN. That sounds sensible. You, in effect, say that the European Economic Community is trying to make priorities out of toxic versus nontoxic and you are going to, in a sense, borrow from their findings and you have been able to identify as a result of their work most of the toxic substances, is that right?

Dr. ELDER. Yes, sir. As a whole, we have been leading. We send more data to Europe that they are using, than reverse. We have an active data exchange.

Chairman WYDEN. I find that hard to see how you get all this data because the FDA cannot compel it legally. FDA is not getting it in all instances voluntarily. You all cannot verify the test data based on your answer to me, and I am curious how you get all this test data.

Dr. ELDER. I think the best answer, and this goes back to my previous experiences, is we target the data. We say exactly what we want. We do not go out and ask for everything.

Chairman WYDEN. You target frequency.

Dr. ELDER. No; we go to the industry and ask for specific data. We do not go out and say, tell us everything in the world that you know about the ingredient. We state only what we need, such as, we need chronic test data, or we need mutagenesis data. We ask for exactly what the expert panel needs to make a determination. If they feel they have sufficient chronic test data to determine safety, they do not ask for more.

Chairman WYDEN. I heard discussion both at the first hearing and today about methylene chloride and we were told that it ought to be banned because it is known to cause significant nervous system disorders. Yet the CIR board ruled that this chemical was safe.

Now, I must tell you that that is the kind of thing that concerns me because here we have a concrete case. Trying to talk about these things in the abstract is difficult, but based on the information that we received at our initial hearing, there are grounds for concern.

Dr. Young is obviously concerned, and yet you all ruled that it was safe.

Dr. ELDER. There is a caveat.

Chairman WYDEN. Why do you disagree with Dr. Young?

Dr. ELDER. I do not disagree. I do not know how Dr. Young is going to rule.

Chairman WYDEN. He told us today that he already set in motion the order to ban this product.

Dr. ELDER. In hair sprays. The expert panel said that methylene chloride could be safely used, intermittently, in hair sprays, but not continuous. It is approved only for an intermittent exposure.

That is different than continuous exposure. The criteria with which Dr. Young is going to use is what I am most interested in. Whether he uses the chronic test data or the subchronic test data. I will be as interested in that as you are.

Chairman WYDEN. Dr. Young said it was going to be banned. I mean there were no nuances about what intermittent meant, and I think one could employ a battery of lawyers, I am sure, to talk about intermittent and how that might mean something in beauty shops and might mean something different for personal use.

Dr. Young said it ought to be banned, that the evidence showed it was unsafe, but your board ruled that it was safe.

Dr. ELDER. I have to say only what the expert panel concluded. The expert panel essentially in nonlegalese words says that it is safe for intermittent consumer exposure. They did not conclude that it was safe for occupational exposure. Intermittent use would be allowed.

Chairman WYDEN. Is your board concerned about workers as well?

Dr. ELDER. Yes, sir. In that standard, their recommendation would cover both. They make no distinction in their recommendations whether it is consumer or occupational.

Chairman WYDEN. Was there an effort to look at the long-term effects of this particular chemical?

Dr. ELDER. Yes, sir. The panel, if it is weighted in any one way, oncology is weighted the heaviest. We have some very distinguished carcinogenic experts. The chronic data, as the committee has been told, is carcinogenic in one species of a mouse. The additional data that will be——is being studied by FDA is the negative data in other test animals.

When the panel looked at the data, they decided that you could not extrapolate one positive animal study to man with the amount of negative data that was also available. They concluded it was safe for brief intermittent exposure.

Chairman WYDEN. Why do you not get us whatever information you have on that particular chemical? Because there is, I think, nothing more instructive than a particular concrete case, and I would like to know why your board ruled that the chemical was safe and why Dr. Young and the FDA have concluded that it is not.

Now, is it correct that of the 275 ingredients reviewed by the CIR board, only one was judged to be unsafe for use in cosmetic products?

Dr. **Elder**. I mentioned that there is another one coming.

Chairman **Wyden**. But is that correct? Yes or no?

Dr. **Elder**. Yes; that is correct.

Chairman **Wyden**. OK.

Dr. **Elder**. May I?

Chairman **Wyden**. Please.

Dr. **Elder**. When one assesses a condition of use, it means that it is safe for the condition that the panel established, such as it is safe at a concentration of 10 percent. Any use above 10 percent would be unsafe.

So, the qualifications placed upon the ingredients are, in effect, setting very tight boundaries.

Chairman **Wyden**. I am sorry. We have those infernal bells going off today. Excuse me just one second.

Chairman **Wyden**. Doctor, if you would be good enough, could you repeat that last part of your comment?

Dr. **Elder**. When one establishes a concentration limit or a limit such as it may be used only in specific products, you are, in effect, saying it is safe for this use; therefore, you are saying it is unsafe for other uses.

The 30 ingredients that have qualifications are limitations on what the ingredient can be used for. It is safe for that, nothing else.

Chairman **Wyden**. So, what you are saying is that while only 1 of the 275 ingredients reviewed by the board was actually judged to be unsafe, others, in effect, have limitations on them?

Dr. **Elder**. Yes; sir.

Chairman **Wyden**. Is that correct?

Dr. **Elder**. Yes; sir.

Chairman **Wyden**. The subcommittee has gotten some information that suggests that the CIR board is using information that, in effect, supports its conclusion.

For example, the case that we were told about involved a tentative report involving the urea chemical where the assertion was that it was safe in concentrations up to 1 percent and that manufacturers were considering adding higher concentrations if further safety could be obtained. But the board was informed that severe allergic reactions resulted at 1 percent concentration.

Another instance that we mentioned involved the methylene chloride. Is the board not looking at all the information and taking some of this in a selective fashion? Tell me about your urea case.

Dr. **Elder**. The ingredient you are referring to is called diazolidinyl urea. That report was put out as a tentative final report. The information that you are referring was unpublished data from the North American Contact Dermatitis Group.

In the panel's first review and first tentative decision, they did, in fact, establish a 1 percent safe level. In their subsequent review, they reevaluated the sensitive population data you referred to. At its last meeting the panel revised its conclusion. It is being republished within the next week with a concentration limit of 0.5 percent, which is, incidentally, consistent with the current use levels and the EEC position.

Chairman **Wyden**. A remarkable number of policies seemed to have been promulgated in the last couple of weeks.

Dr. **Elder**. I know the comments——

Chairman **Wyden**. I am very pleased to see that we are getting some action and want to note for the record that that was a decision made in the last week as well.

Dr. **Elder**. Mr. Chairman, in fairness to the response, that was a very well known dermatologist who insisted that she be heard. The panel went back and looked again. She submitted a lot of data. So, I think that means the CIR system really does work when people operate within it.

Chairman **Wyden**. You testified, Doctor, that some of the safety testing data has been published, but a significant amount is kept in industry files and is not available for public review, is that not correct?

Dr. **Elder**. Yes, sir.

Chairman **Wyden**. These files are not available to the FDA as well, is that correct?

Dr. **Elder**. That is correct.

Chairman **Wyden**. The CIR board does not express an opinion on the validity or the significance of the data it reviews, is that not correct?

Dr. **Elder**. No, sir. The expert panel does comment on the validity of the data. The statement in my text, you may be referring to, is that the staff does not. Neither myself nor the staff comments on the validity of test data. That is done only by the expert panel.

Chairman **Wyden**. It says the CIR staff does not write or express any opinion on the validity or significance of the data.

Dr. **Elder**. Yes, sir. We do not bias the panel. The expert panel makes that decision and they alone make it.

Chairman **Wyden**. How——

Dr. **Elder**. It is our method of developing a report. The expert panel gets every piece of data, good, bad, and indifferent. They throw a lot of data out, if the data does include test methods that were used the panel throws the data out.

The staff puts everything in the report. If we state the results without the test procedures, the panel will delete the data.

If one reads the staff document, and then looks at the panel document you will see the difference. There is a large difference.

You mentioned the unpublished data. We do have a lot of unpublished data in our reports. Some 40 percent of the animal test data that appears in our reports is from unpublished sources.

Chairman **Wyden**. Does anyone look at the adequacy of the industry test data?

Dr. **Elder**. I am only involved with CIR and the priority list, and the expert panel only looks at it on those ingredients.

Chairman **Wyden**. But you get industry data?

Dr. **Elder**. Yes, sir.

Chairman **Wyden**. Does anyone look at the adequacy to see if it is unbiased?

Dr. **Elder**. Yes, sir.

Chairman **Wyden**. Interpreted properly?

Dr. **Elder**. They do not—the industry does not interpret their data. We only accept raw data with no interpretation. The panel itself looks at the data and makes the interpretation on the ingredient under review.

Chairman **Wyden**. This has been very interesting, and I am going to want to review further exactly what you do. I understand, though, that you and FDA parted company on methyl chloride. We understand that you do not actually test the ingredients. We understand that you do not verify the company's test data. All three of those things are certainly areas of concern to me.

I noted your willingness to work with us on following up on those 884 cases to try to determine priorities and to follow up, and we are going to certainly want to work closely with you.

I think the only other question we had dealt with is whether there was peer review in this industry. Does that take place?

Dr. **Elder**. I can only speak for the CIR Program and the CIR expert panel. The public comment is a type of peer review, but the ultimate peer review would be the journal that we publish the CIR reports in. We have not had a report turned down and, incidentally, the fifteenth edition that I mentioned has been accepted, will also contain the report that you would like submitted to the record on methylene chloride.

Chairman **Wyden**. We are going to have to break for another vote.

Doctor, you have been patient. We will return, let us say, in 10 minutes this time.

Mr. Kavanaugh, you all have been very patient, and we will return in about 10 minutes or so and finish up. Thank you.

[Recess.]

Chairman **Wyden**. The subcommittee will come to order.

Let me thank all of you for your patience, and I gather that all who are at the table are going to be witnesses, is that correct?

All right. Please rise and raise your right hands.

[Witnesses sworn.]

Chairman **Wyden**. Thank you all for your patience.

I am told that there is going to be a committee markup in this room at 3 p.m. and I do not want to cut any of you off before you have made your salient and most important comments, but I think I am going to have to invoke a 5-minute rule on this panel.

We will make your prepared remarks a part of the record in their entirety, but since there are one, two, three, four, five, six, seven, we are talking about a minimum of 35 minutes for this panel alone.

Mr. **Kavanaugh**. Mr. Chairman, if I may, I do not think that will be the case at all, but I do think we would like to present a summary of our longer statements. I do not think you are going to find there are 35-minute statements here at all.

Chairman **Wyden**. All right; Mr. Kavanaugh, all of these witnesses accompany you then?

Mr. **Kavanaugh**. You will find there is another group here, the Independent Cosmetic Manufacturers and Distributors, which will follow us. If I may begin our statements, I will be glad to introduce the people.

Chairman **Wyden**. OK, but is it your desire and that of your associates to have all of you testify?

Mr. **Kavanaugh**. No; I will be testifying for CTFA, with very brief remarks by Mr. Romano.

Chairman **Wyden**. So, there will only be two?

Mr. **Kavanaugh**. From ICMAD, there will be two people testifying as well.

Chairman **Wyden**. The rest are available for questions?

Mr. **Kavanaugh**. That is correct.

Chairman **Wyden**. All right; we will do everything we can to give you the maximum amount of time. Why do you not proceed in the way you think is most appropriate?

## TESTIMONY OF EDWARD KAVANAUGH, PRESIDENT, COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION, INC., WASHINGTON, DC; JERRY McEWEN, CTFA VICE PRESIDENT OF SCIENCE; AND PETER HUTT, ESQ., COVINGTON AND BURLING, WASHINGTON, DC

Mr. **Kavanaugh**. I am Edward Kavanaugh, president of the Cosmetic, Toiletry and Fragrance Association, the CTFA.

Accompanying me are, on my immediate right, Frank Romano, who is chairman and CEO of Key West Fragrance and Cosmetic Factory, and a member of the board of directors of CTFA.

On my far left is Dr. Jerry McEwen, CTFA vice president of science. To my immediate left is Mr. Peter Barton Hutt, a partner in Covington and Burling.

Mr. Chairman, as I said, we have submitted our full statement for the record, and I would like to summarize that at this time.

CTFA is the national trade association representing the cosmetic, toiletry, and fragrance industry. We have an active membership of more than 240 companies, which manufacture and distribute the vast majority of the finished cosmetic products in the United States. More than half our members are small businesses, that is, companies with annual sales of less than $1 million. We are here today to discuss the safety of cosmetic products and will make three major points.

First, cosmetic products are among the safest consumer products available.

Second, the cosmetic industry takes its responsibilities to consumers seriously and has voluntarily initiated many programs to ensure the safety of our products.

Third, the Food and Drug Administration currently has and exercises abundant legal authority to regulate cosmetic products.

Nonetheless, as your July hearing demonstrated, neither cosmetics nor any other consumer products are absolutely safe. We must constantly work to reduce the potential for accidents and misuse to the absolute minimum possible.

In response to the concerns raised at your July hearing, I will announce in my testimony today specific new voluntary industry initiatives that we are putting into place to address these matters.

Let me begin by saying that our members are committed to providing consumers with safe cosmetic products. Chances are excellent that every person in this room has used at least one cosmetic within the last few hours, such as toothpaste, shampoo, deodorant, shaving cream, hair spray, cologne, and lipstick, to name a few.

There is no way to guarantee or to prove complete safety of any product under all circumstances. Cosmetics, like all other consumer products, do occasionally produce adverse reactions. These are generally mild and very temporary. They are also very rare. Our goal is to achieve zero incidents, and we will continue to work toward that goal.

The incidents described at your July hearing were terrible and, like you, I am sorry for those people that were involved. At the same time, the personal tragedies suffered by those individuals are not representative of cosmetic product use.

In fact, overwhelming evidence shows that cosmetic products have a superlative safety record. The data collected by the FDA under its voluntary cosmetic reporting program offers evidence of cosmetic safety. According to the FDA data, there are approximately 1.6 reported reactions for every 1 million products distributed, an outstanding safety record.

When properly understood, data from the Consumer Product Safety Commission's National Electronic Injury Surveillance System, the NEISS System, support the excellent safety record of cosmetics.

On the basis of 761 cosmetic-related incidents treated in 62 NEISS sample emergency rooms in 1987, it was estimated at the July hearing that 47,000 cosmetic-induced incidents occurred nationwide. We believe that figure was much too high, so we have asked an independent statistician to examine the NEISS data. We have already submitted his report to your staff this morning, Mr. Chairman, and we would ask that it be put in the record.

Chairman WYDEN. Without objection, so ordered.

[Information referred to above may be found in the appendix.]

Mr. KAVANAUGH. If FDA or any other Government agency believes that there is a question about an ingredient or that a category of products poses a particular kind of problem, I am calling upon them to bring that to our attention so we can gather and make available the relevant information and find a way to solve whatever problem may exist. We have done that in the past, and we are committed to doing that in the future.

The welfare of millions of consumers depends on the safety of our products. It is a grave responsibility, and we take it very, very seriously. We support a number of effective and highly respected voluntary programs to help manufacturers meet their obligations to market safe products.

The cornerstone of these efforts is the cosmetic ingredient review. Dr. Elder has described the CIR and its accomplishments. I will only add that we are very proud of this industry initiative, which is widely recognized as better, faster, and more cost effective than most other review programs, including the FDA's own OTC drug review.

Your press release alleges that cosmetics contain nearly 900 toxic ingredients, yet the publication on which you are relying, the NIOSH Registry, flatly states that these substances do not need to be avoided. In fact, the list includes many substances that are common in every day life and are in nearly every household in the United States.

Some have been explicitly approved by the FDA and all have been considered by the CIR in developing their priority list. I am calling again on anyone who has evidence that a particular ingredient is unsafe to bring that information to the attention of CIR.

Each of these matters will be thoroughly investigated and the CIR staff and expert panel will reach a prompt decision on the priority of each ingredient.

Like all CIR decisions, this priority decision and any subsequent decision on the safety of the ingredient must be made solely by the independent CIR expert panel on the basis of scientific evidence.

In addition to CIR, the FDA voluntary cosmetic reporting program is an important element of this industry's self-regulation efforts. Under this program, which has been in operation since the early 1970's, cosmetic companies provide the FDA with information on their facilities, on the ingredients they use, and on consumer adverse reactions.

Other initiatives we have taken include CTFA's Technical Guidelines, our Compendium of Cosmetic Ingredient Composition, the Cosmetic Ingredient Dictionary, as well as the Cosmetic Industry on Call, which is distributed to every dermatologist in this country.

Several FDA commissioners have had high praise for the cosmetic industry's voluntary programs. For example, FDA Commissioner Arthur Hayes said:

> The cosmetic industry may be viewed as a striking example of what can be accomplished in the spirit of volunteerism. There has been no epidemic of serious adverse reactions to cosmetics and, in spite of the impressive advances in science and technology, as well as in consumer awareness, Congress has repeatedly seen no reason to amend the cosmetic provisions of the FD&C Act as it has with respect to food and color additives, drugs and medical devices.

Let me briefly address FDA's authority to regulate cosmetics. As we stated, we believe it has abundant authority to be sure that the cosmetic industry lives up to its voluntary commitment to safe products.

The agency, however, has had relatively little need to use its authority because cosmetics are generally composed of extremely safe ingredients—inert, and pharmacologically inactive—and because, when necessary, the industry has acted voluntarily to prevent safety problems.

Most important, FDA regulations require industry to substantiate the safety of cosmetic ingredients and cosmetic products before they are marketed. If there is inadequate safety substantiation or if there is the potential for any type of health hazard, the label must bear a prominent warning.

The FDA can also ban or restrict ingredients for safety reasons, inspect manufacturing facilities, issue regulatory letters, seize products, coordinate recalls, enjoin unlawful activities, prosecute violators.

At this time, Mr. Chairman, I would like to ask Frank Romano to take a few moments to talk about the industry from his perspective as the CEO of a small company in our industry.

[Mr. Kavanaugh's statement may be found in the appendix.]

Mr. ROMANO. Good afternoon, Mr. Chairman.

Chairman WYDEN. Mr. Romano, I did not get identified clearly what company you are with.

Mr. ROMANO. I am about to tell you.

Chairman WYDEN. We usually try and do that first.

Mr. ROMANO. All right.

Chairman WYDEN. Please proceed.

## TESTIMONY OF FRANK ROMANO, CHAIRMAN AND CEO, KEY WEST FRAGRANCE AND COSMETIC FACTORY, INC.

Mr. ROMANO. All right; my name is Frank Romano, I am chairman and CEO of the Key West Fragrance and Cosmetic Factory. Good afternoon.

Chairman WYDEN. Where is that located?

Mr. ROMANO. In Key West, FL. I started this company on a shoe string some 17 years ago in a tiny 800 square foot space. My first day's sales were all of $36. We were doing something right because with luck and a lot of hard work, we have become very successful.

From our modest beginnings in Key West, FL, we have branched out through retail and catalog sales to all parts of the country, including Hawaii, where we have several stores.

We manufacture and market a wide variety of products, including skin care, sun tan, hair, bath, men's products, and fragrances. Our products are formulated and manufactured in our own manufacturing facility adjacent to our headquarters store in Key West.

Mr. Chairman, I invite you to come to Key West and inspect my facility. Every single day, we have the public enter and watch our factory at work. I am confident, Mr. Chairman, that you will be impressed with the quality of its operations and the high standards we follow in manufacturing our products.

As a small business man, I am very grateful for the opportunities this country's free enterprise system has given me, and I am most concerned that my company's products continue to live up to the high standards that my customers have come to rely upon.

I must be candid with you, however. I am alarmed about the atmosphere that surrounded the hearing held here in July. The cosmetic industry, of which I am a member, takes pride in the safety of its products, but isolated incidents are being used to needlessly frighten the American consumer.

Some of the witnesses at the last hearing in July seemed determined to use them as an excuse, to saddle the industry with additional unnecessary regulations. Mr. Chairman, I want to assure you that my company observes the highest quality performance standards in manufacturing our products.

We use proven ingredients that have been substantiated for safety and have stood the test of time. We test every ingredient upon delivery. Our facilities are inspected at both the Federal and State level.

I had a State of Florida inspection last month. We passed with flying colors. Believe me, I can tell you from personal experience that both State and Federal cosmetic safety laws are more than adequate to ensure safe products for our customers.

As a recipient of FDA inspections, I would never characterize FDA as a toothless pit bull. What is more, our safety record is outstanding. Our product complaint record is infinitesimal.

I have never had a lawsuit about my products in the entire 17 years of operation. I have never had a serious complaint. We can point with pride to millions of satisfied customers.

I might add that our company supports and fully participates in the FDA's voluntary cosmetic reporting program.

Imposing unnecessary new regulations on my company simply does not make sense. Why should I spend money to retest proven ingredients that we know are safe? Why should my customers pay for this unnecessary testing? Why should some of my colleagues in the industry not be able to compete with large manufacturers, or, worse yet, risk being put out of business because of a new and unnecessary regulatory scheme?

Why should this country's testing resources be diverted for more important health concerns? Why should more animals be sacrificed to reestablish the safety of proven ingredients?

The cosmetic industry must anticipate and react quickly to changing tastes in fashions and styles. Unwarranted new regulations will cripple our ability to respond in a timely fashion. Millions of women customers will be made unhappy.

Unlike the large companies in our industry, we small business men cannot spread our costs over many millions of sale units.

Speaking for myself and on behalf of my small business colleagues in this industry, I urge you not to hamper an important part of America's economy by imposing needless new regulations.

Thank you, Mr. Chairman.

[Mr. Romano's statement may be found in the appendix.]

Chairman WYDEN. Thank you very much, Mr. Romano.

Mr. KAVANAUGH. Mr. Chairman, if I could continue and conclude my statement at this time?

Chairman WYDEN. Sure.

Mr. KAVANAUGH. Thank you. Having said all of this, let me say that you raised some valid concerns in your earlier hearing. Any injury caused by a cosmetic product is deplorable and of major concern to us, whether it is caused by an idiosyncratic reaction, misuse of a product or an unforeseeable accident.

Even though our products are remarkably safe, we intend to take every reasonable step to make their use even safer. In response to your concerns, and they are our concerns as well, CTFA in conjunction with the National Cosmetology Association, the Independent Cosmetic Manufacturers and Distributors, and the American Beauty Association, is beginning the following new cosmetic safety initiatives. They directly address the concerns raised at your earlier hearing.

First, the cosmetic industry has committed to a new program that will assure that the same ingredient information that appears on retail cosmetic products will also be made available for professional products used in beauty salons. We recognize the right of every salon owner, cosmetologist, and customer to have that ingredient information. We are working on the details of how best to provide this information and will proceed with this new program quickly.

Second, we have begun a study of the existing cosmetology licensing and education laws to determine whether existing State and local requirements are adequate to assure proper handling and use of cosmetic products by cosmetologists in beauty salons.

The current Oregon law is a model, but perhaps even it can be improved. Other States may need additional requirements. We will also review how occupational safety and health laws and right to know laws bear upon this matter.

Our study, which we are undertaking with the other professional trade associations, who are equally committed to the safety of cosmetologists, will determine what approach is best suited to achieve that objective.

We support the active enforcement of these laws and regulations.

Third, we recognize that laws and regulations can only provide a structure within which proper education must be provided. We are therefore reviewing existing education programs for cosmetologists to determine whether they provide adequate instructions about the safe handling and use of cosmetic products.

Once again, we are working with both the professional and other trade associations in the field. There are a wide variety of approaches that can be used. We are committed to the most effective way of assuring that safety problems of this kind, illustrated by your earlier hearing, are kept to an irreducible minimum.

Mr. Chairman, our industry is deeply committed to maintaining and always attempting to improve the safety of our products. We want our safe products to be used safely in a safe environment. You have called to our attention your concerns about this matter, and we are responding. We look forward to working with you and the committee in the future on these matters.

Chairman Wyden. Mr. Kavanaugh, thank you, and, first of all, let me say I think we have some differences of opinion on it, but your association in every respect has been cooperative in working with the subcommittee and with me personally. I want you to know I appreciate that.

Let me also say that these new initiatives that you are announcing today sound very useful. We will await the details, and I think particularly the witnesses that we heard last week will find your interest in trying to make sure that the same ingredient information that is on most retail products gets on these products in beauty salons, will be appreciated, and I think there are a lot of cosmetologists, salon operators, and owners who are going to appreciate that.

When do you anticipate—just one question on that—when do you anticipate having this new program up and running?

Mr. Kavanaugh. We have already begun working on part 1 which is, I think, the prime issue that you wanted us to address, and that is the ingredient information being made available for professional products.

I would think in the next 3 to 6 months, we could have agreement on how to do that. Certainly it will be done faster voluntarily than any other method that could be employed.

Chairman Wyden. Let me say personally, my inclination would be very much inclined toward giving you the chance to do that voluntarily. It sounds very useful. Would you please keep the subcommittee apprised as you go along?

If you feel you can have that up and running in 3 to 6 months, I think that would be useful.

Let me turn now to some areas where there is some disagreement and see if we can try to lay out what those are.

I asked Commissioner Young specifically, slowly, and carefully whether there was a statutory requirement that cosmetic ingredients be tested for safety before they were used. Frank Young said there was no statutory requirement.

You have said and told me in conversations we have had that the cosmetic industry is required to test individual ingredients in finished products.

That seems to me to be a 180 degree difference between what Dr. Young said in sworn testimony and what you have said.

Try, if you will, to shed some light on why there is such a difference of opinion on that point.

Mr. KAVANAUGH. There is a legal obligation that was issued by FDA in March 1975 for all manufacturers and distributors of cosmetic products to substantiate the safety of their products prior to marketing. That is a legal obligation that, if not met, requires the label of the product to bear a warning statement that says the safety of this product has not been determined.

Chairman WYDEN. Why would Dr. Young indicate otherwise? Because he said, and I asked him very carefully and I think you were there, that there was no statutory requirement that an ingredient be tested for safety before it was used? I asked that question for a reason. I asked it to——

Mr. KAVANAUGH. He added, Mr. Chairman, that products otherwise would have to bear a warning, and I think it might——

Chairman WYDEN. Well——

Mr. KAVANAUGH. If you would let me finish.

Chairman WYDEN. Please.

Mr. KAVANAUGH [continuing]. The difference here, I think, is over tested and substantiated, which may be a matter of semantics. The legal obligation is to substantiate the safety of these products prior to marketing. Otherwise, as Dr. Young said, the label of the product must bear a warning that the safety of this product has not been determined.

Chairman WYDEN. I——

Mr. KAVANAUGH. If you go on to the safety of the ingredients, we are handling that through the cosmetic ingredient review, which you have heard about.

Chairman WYDEN. What I heard——

Mr. KAVANAUGH. That goes a long way to substantiate the safety of the product by having the safety of the ingredients substantiated.

Chairman WYDEN. I did not find encouraging what I heard because the CIR representative, Dr. Elder, told me specifically that they did not test for ingredients.

So, what we have on the record here, and this is sworn testimony, is that Dr. Young said there is no statutory requirement that an ingredient be tested for safety before use. Dr. Elder said that he was not testing ingredients for safety, and I am still unclear as to how these ingredients get tested for safety before use.

Now, your point with respect to the warning, I presume, is relevant to this. No one disputes that, and I want to make that clear. But that is not the same thing as a legal requirement that ingredients in cosmetics be tested for safety before use.

Mr. KAVANAUGH. The safety substantiation regulation as issued points out what constitutes that substantiation. It cannot be done in the absence of information. It must be done based on data, and data on the ingredients would be test data.

Chairman **Wyden**. I can tell you only that in addition to what Dr. Young said, the last time the FDA had a task force on cosmetics, they concluded exactly what Dr. Young said today, which was that there was no statutory requirement that ingredients be tested for safety before use.

Mr. **Kavanaugh**. The agency issued that regulation under the Federal Food, Drug, and Cosmetic Act. It is a regulation that was issued under section 201(n) of that act, which requires full disclosure of any material fact. I do not think there is any disagreement between or among the three people you have quoted.

Mr. **Hutt**. Mr. Wyden, there may be some confusion because your question is whether there was a statutory requirement.

That requirement was not in the statute; it is in the implementing regulations issued under the statute.

Chairman **Wyden**. Why do you not read me then the legal requirement that ingredients be tested for safety before use?

Mr. **Hutt**. Here it is. It is section 740.10 of volume 21 of the Code of Federal Regulations, which states, and Dr. Young paraphrased it:

> Each ingredient used in a cosmetic product and each finished cosmetic product shall be adequately substantiated for safety prior to marketing. Any such ingredient or product whose safety is not adequately substantiated prior to marketing is misbranded, unless it contains the following conspicuous statement on the principal display panel, WARNING: The safety of this product has not been determined.

That is a direct reading of that regulation——

Chairman **Wyden**. All right; that then goes to the question of how it is determined that there is adequate testing, and we had again on the record that the Food and Drug Administration does not have the legal power to compel companies to hand over test data. Dr. Young went further, contradicting what your association told me, that there were many instances where companies did not hand data over to the FDA when they asked for it voluntarily.

Mr. **Kavanaugh**. I think that Dr. Young did not say, however, Mr. Chairman, that companies refused to hand over data when there was a serious concern about safety. I do not think Dr. Young said that.

Chairman **Wyden**. I asked specifically whether there were many occasions where companies refused to hand over test data to the Food and Drug Administration, and Dr. Young answered yes.

Mr. **Kavanaugh**. As you know, FDA does not have authority to do that. The point we made to you before, and I will make again, is that whenever FDA has asked for information from a company, to the best of our knowledge, they have given it to the FDA when there is an appropriate reason to do so.

Chairman **Wyden**. That directly contradicts what Dr. Young said.

Mr. **Kavanaugh**. I do not think it does.

Chairman **Wyden**. Mr. Kavanaugh, that is exactly what it does. Dr. Young said there were many occasions where companies did not hand over test data to the agency. That will be on the record. It is sworn testimony and contradicts what you said here. It also contradicts what I was told in the office.

Mr. **Kavanaugh**. No; I do not think it does. I do not think that Dr. Young indicated that whenever he had a need for safety reasons, that he expected a hazard, that he could not get that information.

If so, Mr. Wyden, as I said to you in your office, and I will say to you here——

Chairman **Wyden**. You are——

Mr. **Kavanaugh** [continuing]. I would like to know what those cases are.

Chairman **Wyden**. You are now making qualifications which are not what I asked Dr. Young about. They may be interesting, but what I asked Dr. Young about specifically was the question of whether test data could be legally required by the FDA and he said no, and whether FDA was able to get it voluntarily and he said, on many occasions they could not.

Now, you have added something that I did not ask about. It is interesting, the question of whether in instances when the industry designates important safety questions, it would be handed over to the Food and Drug Administration.

I must tell you that I think it unlikely that people will hand over information in these instances that you describe, and I consider it even more unlikely based on what Dr. Young said today. I was very pleased that he indicated he was going to make a strong push for additional voluntary disclosure of this, and I consider that very important.

I want to put you on notice right now that if there is not an effort to comply with what Dr. Young said was important today—which is to be able to get this data voluntarily—then we are going to be talking about a legislative approach. I made it clear to you that I want to see what we can do voluntarily, but a number of things I have heard today, and that was just one of them, did not exactly give me enormous confidence in the voluntary program.

For example, at the last page of Dr. Young's testimony, he cites the data with respect to industry participation in voluntary cosmetic programs. In a number of these instances, participation is well under 50 percent.

Now, I am going to tell you again that I think you are going to have to get voluntary participation up dramatically. Dr. Young made that clear as well—if you want those of us in the Congress and the public to be satisfied with it. Do you think these numbers are acceptable?

Mr. **Kavanaugh**. Let me answer that, and then I would like to go back to the previous point.

Chairman **Wyden**. But tell me first if you think it is acceptable to have 14 percent of those involved in filing and amending formulations since 1984 to comply.

Mr. **Kavanaugh**. The voluntary program participation covers about 80 percent of the volume in this industry, which we think and FDA has stated—FDA Commissioner Arthur Hayes stated in 1983—provides tremendously valuable information. Eighty percent of the industry responding provides FDA with adequate information about trend analysis or to spot areas where there may be a problem.

I will tell you, Mr. Wyden, that I will agree with Commissioner Young, and we will work harder to get that participation up, but nonetheless, the Commissioners have stated that it is very useful information to get. We will try to make that better.

Chairman WYDEN. I appreciate what you are saying about getting the participation up, and——

Mr. KAVANAUGH. If I may add to that, there are a lot of small companies, because of the red tape of the forms, which are not easy to fill out, that are not participating. But I must say also that of the establishment numbers that were given to you this morning, and as you will hear when the ICMAD testifies, many of these companies are not manufacturers. Rather, they are distributors and therefore are not registered in that program.

Chairman WYDEN. A couple of things. Did not your organization write these voluntary forms? These were not written by the FDA, were they?

Mr. KAVANAUGH. We submitted petitions to the Food and Drug Administration which were then available for public comment. The public comments were made and the FDA adopted these regulations in the Code of Federal Regulations.

Chairman WYDEN. But the fact is that the instigator in terms of developing these voluntary forms was your association and compliance is still very, very low in most of these key kinds of areas.

Mr. KAVANAUGH. Not by volume, Mr. Chairman. We are representing about 80 percent of the industry by volume. What you are talking about is a numbers game, and I am telling you that many small companies who are distributors, not manufacturers, are not registered because they are not required to register.

Chairman WYDEN. We are not playing any numbers games, Mr. Kavanaugh. These were furnished by the Food and Drug Administration. Dr. Young today said he was dissatisfied with the levels of voluntary participation.

I hope that you all are going to get the message because that is one of the things that I am looking at in terms of really reviewing our progress in this area.

Now, with respect to small companies, and I want to be clear on this as well. I am prepared to be very sensitive to the concerns of small companies in terms of filing forms and various kinds of requirements. I have sat on this committee and sponsored legislation in a number of areas to try to hold down the kind of unnecessary administrative baggage, if you will, and we are prepared to be very sensitive to that.

But I looked at those numbers of Dr. Young and asked him about them for a reason. He said he was dissatisfied. I am as well.

Now, we can certainly look to streamline procedures in terms of smaller companies and be very sympathetic——

Mr. KAVANAUGH. We will continue our efforts to work with FDA to increase that participation. I also think that Dr. Young pointed out that he had sufficiently useful information so that he could issue a warning statement, for example, on children's bubble bath products.

Chairman WYDEN. I am sorry? What was that?

Mr. KAVANAUGH. He had sufficient information from this program to make regulatory decisions. Commissioner Hayes made the same point in 1983 and that is because, Mr. Chairman, of the volume that is there.

We will try to get the number of companies that will voluntarily submit their information to FDA to increase.

Chairman WYDEN. I appreciate that, and that is one of the goals of this subcommittee. Let me state again, over the next few months, that is one of the key things that I am going to be looking at, to see that those voluntary numbers go up. Let us see if we can get in another question before we have a break.

One of the other things that Dr. Young talked about that concerned me greatly was an issue that grew out of the inspection process, and what the FDA staff told us, "The agency usually discovers absence of safety substantiation at the time a product is found hazardous," and I said and Dr. Young essentially agreed that that raises some questions about the existence of adequate testing data.

Are you prepared to take additional steps voluntarily to beef up the substantiation so that the FDA will not, when they go out there, find an absence of safety substantiation?

Mr. KAVANAUGH. Let me go back to 1975 when that regulation was issued. Our response to that program, Mr. Chairman, was to develop the Cosmetic Ingredient Review Program because safety substantiation goes to both ingredients and the finished product. We thought, through the industry association, we could set up a program to establish the safety of the ingredient.

We also knew that, if it was going to be a credible program, it had to be an open process, and that is why it is an independent review. That program is well along the way of looking at the most frequently-used ingredients that are most biologically active. Those are the criteria that are established.

So, we have responded in that way with that program. The companies have a legal obligation to substantiate the safety of their products prior to market. Much of that information is available through the cosmetic ingredient review. The companies then have the burden to substantiate the safety of the finished product prior to marketing.

Chairman WYDEN. Yes; but that contradicts what the FDA said. The FDA said in writing that the agency usually discovers absence of safety substantiation at the time a product is found hazardous.

Mr. KAVANAUGH. I do not know of one instance where that is the case.

Chairman WYDEN. So, you disagree with the FDA on that?

Mr. KAVANAUGH. I would like to know what he is talking about because we do not have any such information.

Chairman WYDEN. We are going to follow up on that point, and we will communicate with you about those specific instances.

We have a vote on the floor. We will therefore break for another 10 minutes.

[Recess.]

Chairman WYDEN. Mr. Kavanaugh and your associates, again, my thanks for your patience and hopefully we will get a few minutes in.

With respect to the labeling that cosmetic products must comply with, are these labeling requirements that clearly lay out on the package what the ingredients are or do these essentially go to that descriptive sheet that you can find somewhere else?

Mr. KAVANAUGH. Are you referring to our——

Chairman WYDEN. Yes; with respect to what you are proposing.

Mr. KAVANAUGH. We are looking for the best way. I expect, Mr. Chairman, that some companies will choose to put it on the label; other companies will have it either as a tag with the product or in some other way accompanying the product.

I think there are many ways. It is being done now, as you know, under the OSHA Hazard Communication Standard, but we, as we indicated in this program, intend to go much beyond that, to provide 100 percent communication to the salons.

Chairman WYDEN. With respect to the ingredient issue, which I think is contentious and is going to continue to be, would your association be willing to give to the Food and Drug Administration information attesting to ingredient safety?

Mr. KAVANAUGH. I am sorry. I did not hear the last part.

Chairman WYDEN. Would your association be willing to give on a voluntary basis information to the Food and Drug Administration that attests to ingredient safety?

Mr. KAVANAUGH. Most of that information you will find available today in the cosmetic ingredient review. All those materials and raw data are in the public domain, covering nearly 300 ingredients that have been reviewed.

I think that, as you know and heard Dr. Elder say, covers some of the most commonly-used ingredients in the industry for which the safety substantiation already exists and is public.

Chairman WYDEN. Again, you have said that it is available through the CIR, and I asked specifically whether they tested for ingredients and they said they did not. So, we have a difference of opinion on that.

Would you be willing to give information that would attest to ingredient safety as part of the product substantiation process?

Mr. KAVANAUGH. The safety substantiation requirement requires that it be substantiated prior to marketing.

Chairman WYDEN. It does not say that that information must be given to the Food and Drug Administration.

Mr. KAVANAUGH. That is correct.

Chairman WYDEN. Would you be willing to give that information to the Food and Drug Administration?

Mr. KAVANAUGH. We do it now for a great part. Whenever FDA asks, when there is a problem, and, second, when the ingredient information is available under the CIR Program.

Chairman WYDEN. They, of course, said that there were many instances where they asked and they did not get it. Why do we not say——

Mr. HUTT. Mr. Wyden, I would like to suggest——

Chairman WYDEN [continuiing]. Let me finish my sentence, if you would.

What I would like to ask is whether the association would be willing on a voluntary basis to give that information with respect to safety substantiation to the Food and Drug Administration.

Mr. KAVANAUGH. The answer to that question is that it is not a part of the law. I can only answer the way I have, Mr. Chairman.

When there is a serious situation, any question that FDA has, not a fishing expedition——

Chairman WYDEN. I am going to interpret that as saying no. You are not willing on an ongoing basis to give safety substantiation to the Food and Drug Administration. We are not talking about a bill. It is not a legislative requirement. What we are talking about is on a voluntary effort, giving safety substantiation information to the FDA.

Mr. KAVANAUGH. When a company is asked, I am sure that it will do that.

Chairman WYDEN. But that is not being done, Mr. Kavanaugh. You were here. You sat in the front row when Dr. Young said that it was not being done.

Now, I am not going to get back into it because his testimony is on the record. What I want to know is whether on a policy basis, ongoing, your association is willing to give safety substantiation data to the FDA.

What I have heard today is that you are not willing to do that on an on-going voluntary basis.

Mr. KAVANAUGH. All the information that is available through CIR, we will be glad to submit to FDA.

Mr. HUTT. Mr. Wyden, perhaps I could offer some clarification. In 20 years, to the best of CTFA's knowledge, FDA has never once asked for safety substantiation data from CTFA and been turned down. Never. We have given it in the past and we will give it in the future.

Chairman WYDEN. What test data was Dr. Young talking about?

Mr. HUTT. What Dr. Young said, and I have sought clarification from Mr. Eiermann during the break, was that there are occasions when FDA inspectors will ask for some type of information on a factory inspection from a company and it will not be provided.

But Dr. Young did not say that, and Mr. Eiermann could not give me a single incident, where an inspector has been sent by the FDA to a company and said, we have a specific safety concern about a particular ingredient or a designated reason, the company has turned them down.

I told you in your office, and I will repeat today, I know of numerous incidents like that where the company has turned over the information promptly to the Food and Drug Administration. I know of incidents where that has not only occurred, but FDA has subsequently asked the company to recall the product and they have recalled it.

Chairman WYDEN. You simply are trying to rewrite the record, and I am not going to accept that.

I asked Dr. Young specifically whether there were many occasions where companies have refused to disclose testing data to FDA, and he answered yes. It is that simple and that——

Mr. HUTT. There are all kinds——

Chairman WYDEN. It is unfortunate that on a policy basis, we cannot get the industry to voluntarily give safety substantiation data to the FDA.

Mr. HUTT. Mr. Wyden, we can get the industry to do it voluntarily. They do it voluntarily today. We are going to seek immediately after this hearing clarification from FDA about the type of circumstances under which information has been denied.

We have said, and Dr. Young in his statement said, that where there is a general fishing expedition, he can understand it might not be turned over, but where there is a particularized safety concern, I am not aware, and he cited no specific instance, that data that is important to public health has been denied.

Again, we testified today, CTFA has never once in 20 years of my personal knowledge declined to give that kind of information, and we will not in the future.

Chairman WYDEN. The only question I wanted to ask, and I would ask more except our time is short, what would be wrong with a policy change requiring companies to tell FDA about consumer reports of adverse reactions?

I asked about that issue specifically with Dr. Young. Would you be willing to support a policy change in that area where companies would have to tell FDA about consumer reports of adverse reactions?

Mr. KAVANAUGH. It is a voluntary regulation. If companies are asked for those, they will turn them over.

Chairman WYDEN. But there is no legal obligation. I asked Dr. Young that specifically and he said there was no legal obligation.

Mr. KAVANAUGH. There is not. There is not with food. There is not with OTC drugs.

Chairman WYDEN. Would you be willing to support a policy change where companies would have to tell FDA about consumer reports of adverse reactions? Yes or no?

Mr. KAVANAUGH. The voluntary program procedure in place is a good one. If a program is proposed that would follow along those guidelines, we certainly would be willing to discuss that.

Chairman WYDEN. The other question, and we may be going down the same road, is that Dr. Young said there was no requirement that companies have to register their manufacturing establishments or product formulations with FDA. Would you support a policy change for that sort of requirement?

Mr. KAVANAUGH. As I indicated before, Mr. Chairman, about 700 establishments are registered, and there are 20 odd thousand formulations on file with the Food and Drug Administration which supply to FDA sufficient information, as I think the last three or four Commissioners have stated. As I had mentioned to you, we will try to do better. We will encourage our companies to submit and keep their formulations up to date.

I think part of the problem, when you looked at that figure before that you cited, and as Mr. Romano pointed out to me, he has not changed many of his formula filings in many years because his formulas have not changed——

Chairman WYDEN. I did not want to cite just one figure. When you look at all the figures for all the programs, that you all say work so well and are purely voluntary, participation for most of them is well under 50 percent.

Mr. KAVANAUGH. It still covers about 80 percent of the volume of the industry. As far as those numbers are concerned, we will try to get them up. We will work with FDA to do that.

Chairman **Wyden**. We are going to leave the record open, I think, at this point simply because we have three remaining witnesses.

Mr. **Kavanaugh**. You also have the National Cosmetology Association which has been sitting here throughout the day as well.

Chairman **Wyden**. This requires some ingenious thinking here. I thought you and your associate, Mr. Romano, had finished their presentations.

Mr. **Kavanaugh**. We are finished if you are finished.

Chairman **Wyden**. Mr. Kavanaugh, we may have mutual interests satisfied here. Would it be acceptable to excuse your panel at this time?

We are going to hold the record open, Mr. Kavanaugh, as well for some of these additional areas we want to talk about to you all and also some written questions we are going to want to submit.

Mr. **Kavanaugh**. We would be glad to respond.

Chairman **Wyden**. Thank you. All right. My apologies to our last witnesses, Mr. Lightman, Ms. Baden, and Mr. Byerley. We did not anticipate going on this long. We will put your remarks into the record in their entirety. If you could perhaps summarize some of your key concerns, that would be of great help.

## TESTIMONY OF WINNIE BADEN, PRESIDENT, ROSE LAIRD COSMETICS AND BOARD MEMBER, ICMAD; ACCOMPANIED BY HAL LIGHTMAN, PRESIDENT, I.S. LABORATORIES, INC., FOUNDING MEMBER AND FORMER PRESIDENT, ICMAD, AND WALTER E. BYERLEY, ICMAD LEGAL COUNSEL

Ms. **Baden**. Congressman Wyden, members of the committee, thank you for inviting our association to participate in this hearing, covering cosmetic safety.

I am Winnie Baden, a director of ICMAD, the Independent Cosmetic Manufacturers and Distributors, a nonprofit trade association of more than 500 companies, located in 35 States. I am also president of Rose Laird Cosmetics, a New York-based company in continuous commerce, selling many millions of skin and hair care products since 1912. Prior to 1968, we sold products in better department stores and in our salons on Fifth Avenue and Park Avenue. For the last 20 years, we have sold through direct mail.

Rose Laird, just as many other cosmetic companies, does not make its own products. We do however, have our own formulas and we oversee the manufacturing and personally test each new batch.

From personal experience during my 6 years as a board member of ICMAD, I have found that our membership represents concerned individuals who wish to provide the purest, safest products at the most economical prices. We are all, in addition, very dependent upon the look, the feel, and the effectiveness of each and every product. Every one in the cosmetic and personal care industry is truly concerned about the products we place on our faces, on our hair, and on our bodies. We all use these products and we all police ourselves as individual manufacturers, distributors, and consumers in order to keep industry products safe.

One of the purposes of a trade organization such as ICMAD is to provide its members with an opportunity to share the experiences and knowledge about reputable private label companies who employ competent cosmetic chemists, who insist on good manufacturing practices, and who test final formulations. These practices include the use of approved ingredients, microbiological testing of each batch, and skin testing for possible reactions.

ICMAD's members are primarily smaller cosmetic companies who do not have the legal and technical staffs of the larger companies. ICMAD makes certain, therefore, that members promptly receive new relevant information as it becomes available. Professional assistance is provided through our legal counsel, intraassociation hotline, monthly informational publications, and bulletins that cover every critical issue, whether it affects one member, or the entire industry.

Since 1983, ICMAD has worked closely with the FDA in cosponsoring a continuing series of Cosmetic Educational Workshops. Our joint purpose has been to keep smaller companies informed and up to date on all regulatory and legislative matters. Attendance has been excellent. More than 100 companies, both members and nonmembers, have enthusiastically attended each seminar.

On November 1, 1988, ICMAD will cosponsor with the FDA our ninth workshop in New Orleans. These seminars have been conducted previously in New Jersey, Florida, Texas, Illinois, and California. Copies of our printed material and workshop agendas have been provided to this committee.

The documents this committee has accumulated and the figures which are not actual but extrapolated all indicate that the issue is not the safety of the products which the cosmetic industry manufactures for the retail market, but rather, how the products are professionally used in the workplace and how products to be used by professionals only, should be labeled.

Over the years, a mass of data has accumulated which clearly places cosmetics among the safest consumer products on the market. This is particularly so considering the number of consumers, the frequency of cosmetic use and the very low percentage of insurance claims filed. Rose Laird, for example, among its more than 300,000 clients, has had no adverse reactions reported for the past 50 years.

ICMAD believes that every effort should be made to improve the working conditions of beauty professionals who are exposed to certain chemicals almost every day of their lives. It should be assured that, as professionals, they have been instructed on the nature of their industry products, and how and where to use them. Beauty professionals should receive instruction on the flammable nature of many of the products they use professionally and the need to prohibit smoking within their work environment, and also, because cigarettes are considered a carcinogen.

ICMAD supports the use of ingredient disclosure for all products sold for professional use in the beauty industry. Appropriate warnings clearly printed on labels should be mandatory. OSHA already has mandatory standards for beauty salons, and these standards can, and should be enforced by the board of health in every community.

ICMAD maintains that further regulations on the cosmetic manufacturing community are unnecessary and would only promote a hardship for small business owners. For every manufacturer in the industry, large, medium, and small, the financial cost to implement additional changes, as has been proposed, would lead to price increases on products that already are becoming out of reach and, most important, it is questionable that a safer cosmetic environment would be achieved.

These restrictions would, in addition, severely burden the small business segment of the cosmetic industry, and without a doubt shrink the number of entrepreneurs, the lifeblood of our association and of our country. Thank you.

[Ms. Baden's statement may be found in the appendix.]

Chairman Wyden. Ms. Baden first of all, you said that there had been proposals to put burdens and restrictions on the industry. No one to my knowledge has made any such proposals. Certainly I have not. These are hearings to assemble the facts, and I want the record to be clear on that point.

We are going to have to move over to the next room, room B. It is kind of an emergency hearing room surgery. We are going to be able to get about two-thirds of those who are in the audience now in that room over there.

I do not want to say first come first served and cause a brawl here, but if you are willing to be patient with us, we will start over there in about 10 minutes.

[Recess.]

Chairman Wyden. Subcommittee is called back to order.

First, I want to thank our recorder, who has come on incredibly short notice, and I want to personally thank her for her assistance. I have been in Congress now for 4 terms and I do not think we have ever once run up against this predicament, and I want our recorder to know that the Chair is very appreciative of her coming. I think it is a real compliment to the fine work that you all do that you have been able to assist us in this fashion.

Let me also apologize to our witnesses for the inconvenience, particularly to you, Ms. Baden. You barely got the last word out of your mouth before we had to leave. I appreciate it.

We are now well situated for time, I think, though I would still like to ask our witnesses to summarize.

Mr. Lightman, you have already been sworn in. We will make your remarks part of the record, and if you could summarize your concerns, that would be helpful.

[Witness sworn.]

## TESTIMONY OF HAL LIGHTMAN, PRESIDENT, I.S. LABORATORIES, INC., FOUNDING MEMBER AND FORMER PRESIDENT, ICMAD

Mr. Lightman. Chairman Wyden, one, may I thank you for making these special arrangements, going to all this trouble.

My name is Hal Lightman. Fifteen years ago, I was one of the founders of ICMAD and have spent 30 years in different facets of the cosmetic field. At present, I am president of I.S. Laboratories, a small family-owned cosmetic company.

In 1974, 11 concerned men and women, all owners of small cosmetic businesses who believed in the American dream, formed the

Independent Cosmetic Manufacturers and Distributors to represent them and to protect the small entrepreneur's interests.

These original 11 have grown so that today ICMAD represents more than 500 member companies in over 35 States. It includes minorities, blacks, Mexican-Americans, Asiatics, Spanish-Americans, single parents, veterans, and senior citizens.

ICMAD members have available to them in many instances the same technical sources to protect the public health as the major publicly-owned cosmetic companies. All of us have the results of toxicity testing on ingredients, and we all use only those ingredients found to be safe.

Many use the same laboratories for testing finished cosmetic products, including microbiological testing, batch and challenge testing. I personally used the same testing laboratories for this type of safety testing of cosmetic products for my companies as do the giants of the industry.

The small entrepreneur, in addition to Government regulations, has other great incentives to produce safe products, namely to protect his customer and to avoid product liability exposure. In today's litigious climate, any manufacturer would be a fool not to comply with all Federal regulations. If proper recordkeeping and housekeeping practices are not followed, a company's very existence is jeopardized.

Everyone agrees that there is no such thing as a zero risk product. Everyone accepts that somewhere, sometime, someone will experience a skin reaction in her or his use of a cosmetic. Of course, we are concerned about every incident, but more regulations will not prevent the misuse of or allergic reactions to any product.

ICMAD feels that current FDA regulations covering the cosmetic industry are more than sufficient to protect the public. Many of our members are beginning to export for the first time, which can help reduce the balance of payments, the deficit, and create new jobs. But, this will be strangled by unnecessary additional regulation as would be our very existence.

ICMAD would like to note that the testimony of the two cosmetologists who appeared before the committee on July 14, 1988, actually dealt with poor ventilation. We deplore the working conditions that these workers described, and applaud the union if they brought these experiences to OSHA for immediate remedial action. That is, of course, where they would and could solve the problem as described.

However, we trust the committee will disregard the other statements of Beth Schulman, the vice president of Professional Hair Care and Beauty Trades, which were unfounded.

These allegations about the entire cosmetic industry, unsubstantiated by facts, we deplore. They question the integrity of our many small business entrepreneurs. They are extravagant and biased, and we feel certain the committee will see them for what they are, simply—headline seeking.

ICMAD deplores the seizing upon isolated incidents to brand an entire, safe industry as dangerous and irresponsible. ICMAD urges the committee to place the testimony given by previous witnesses and the alleged injury statistics they extrapolated in true perspective against the broad safety record and the actual experience of the entire cosmetic industry.

We support existing FDA requirements and we follow them. We join CTFA in supporting a program to provide ingredient information in beauty salons for professional products.

Finally, we repeat, ICMAD and its individual members are totally committed to protecting the consumer. ICMAD and its individual members are firmly opposed to any additional restrictive legislation that increases the costs of our products, without benefit, to the consumer. That threatens the survival of many of the small cosmetic companies.

ICMAD as an association of small cosmetic businesses is prepared to offer its full cooperation to the Small Business Subcommittee in its effort to protect and ensure product safety in the workplace and in the home.

Please, do not be like the friend who puts a tourniquet around his associate's neck to stop a nose bleed. Thank you, sir.

Chairman Wyden. Thank you very much, Mr. Lightman.

Mr. Byerley.

Mr. Byerley. I am here as counsel.

Chairman Wyden. All right. Very good. We will then permit you to advise your clients. Is your client Ms. Baden, Mr. Lightman, or both?

Mr. Byerley. The association.

Chairman Wyden. Very good. Ms. Baden, my sense is that ICMAD has changed its position on this ingredient labeling matter.

I have a newsletter from the association that talks about ICMAD's history. It starts off:

> 1974 to 1988, ICMAD grows from 8 to almost 500 members. Early in 1974, a group of small cosmetics manufacturers became concerned over proposals by the FDA to publish regulations requiring ingredient listing on cosmetics products.

It then goes on and talks at some length about the history and the like.

What I am most concerned about is essentially the discussion at the end of the first page in the newsletter where it says, "ICMAD succeeded in delaying effective date of the law," speaking of ingredient labeling legislation for 2 years. It appears that at that time, ICMAD was really touting the fact that it put considerable resources and considerable emphasis on trying to kill ingredient labeling legislation.

Now, in your testimony today, you all have changed position. Is that a fair statement to make?

Ms. Baden. I was not a member at that time, and I do not know that I can address that.

Chairman Wyden. Mr. Lightman?

Mr. Lightman. Yes; I can. The answer is yes; we came down here because as it was originally proposed, the ingredient labeling could have and would have seriously damaged the small business man and woman.

We were against it since it did not benefit the consumer and would increase prices. We did our utmost to correct this. We sat down with the committee, as we hope this committee will do with us in the future, worked it out so that it could work effectively.

When it finally became the law of the land, we absolutely adopted it and every one of our members immediately put the ingredients on their packages.

Chairman **Wyden**. I am pleased to see the change of position or what appears to be a change of position, although some comments have been made in California, I think, that raise some questions as well with regard to proposition 65.

Those comments indicate that ICMAD would argue against specific label warnings on each product and work to urge a warning procedure that would keep the warnings general and as far removed from individual products as possible. Do you know anything about that?

Mr. **Lightman**. No, sir, I do not, but I can find out for you.

Chairman **Wyden**. Would you find out for me?

Mr. **Lightman**. Yes, sir. Absolutely.

Chairman **Wyden**. It is in the ICMAD newsletter analyzing the implementation of the California statutes. So, I am anxious that you all will support what you appear to say in Ms. Baden's statement, which is that in a straightforward way, you all will support ingredient disclosure for products sold for professional use. I must say that I was concerned, having read the newsletter that summarized the history from 1974 to 1988, and I was a bit more concerned when I read the comments that were in one of the newsletters with respect to the California statute.

Now, I personally have some questions about a number of aspects of the California statute, and we are not here to debate the California statute or parts thereof, but I hope that you all will support what appears to be in the statement, which is the need for full ingredient disclosure and labeling.

Mr. **Lightman**. Congressman, I do not believe in volunteering, but may I add one thing?

Chairman **Wyden**. Sure.

Mr. **Lightman**. Fourteen years have passed and changes that happened in the marketplace during those 14 years can change your opinions and changed circumstances affect what you will go along with.

Chairman **Wyden**. That is encouraging, but, again, this California newsletter is pretty recent and reflects what seems to be a major policy statement, and that is why we felt compelled to ask about it.

How many of your member companies, Mr. Lightman, have voluntarily registered with the FDA?

Mr. **Lightman**. A great many of them have, sir. I cannot give you the exact number. I believe that most of the plants do.

Chairman **Wyden**. Why do you not provide that for the record as well? How many of your members have registered formulation data with the FDA?

Mr. **Lightman**. The same would apply, sir.

Chairman **Wyden**. A great many?

Mr. **Lightman**. To the best of my knowledge, yes; sir, but I can check it and add it to the record.

Ms. **Baden**. I know that my company does.

Chairman **Wyden**. Has registered?

Ms. **Baden**. Yes.

Chairman **Wyden**. How many of your members report consumer product complaints to the FDA?

Mr. **Lightman**. When and if there are any, to the best of my knowledge, they also do that. We adhere as closely as possible because we feel it is in the best interests of our companies.

Chairman **Wyden**. You have been in the business for 14 years. Longer?

Mr. **Lightman**. Thank you. No; 30.

Chairman **Wyden**. Since you have been on the board, let us take that period, have you reported consumer product complaints to the FDA during the 14-year period?

Mr. **Lightman**. I think one or two that occurred in our company that I know of, that I can speak for. I cannot speak for anyone else. They were of a very minor nature.

Chairman **Wyden**. We will hold the record open to get that additional data. If you all do not have anything additional you would like to add, we appreciate your coming.

I also want to say, as I said earlier, that I have considerable sympathy for the administrative requirements that can be imposed on small businesses for little or no good. We will be particularly judicious and particularly careful about looking at what any initiative will mean for small businesses.

Ms. Baden, that is why I reacted when you said you were unhappy about burdensome regulations that had been proposed. There have been no burdensome regulations proposed, at least by the chairman of this subcommittee, in fact, there have not been any regulations proposed at all.

We are in the process of trying to collect the facts and consider the arguments that you have made and, frankly, I do not know if he is still here, but Mr. Romano with respect to small businesses, I think, are well taken, and we appreciate your cooperation with the subcommittee. We will excuse you at this time.

Ms. **Baden**. Thank you.

Mr. **Lightman**. Thank you very much, Mr. Chairman.

Chairman **Wyden**. Cis Stock Kennard, legislative chairman, National Cosmetology Association. Thank you both very much for your patience. It has been an awfully long day, and we are glad to have you with us. You have been kind to wait.

Ms. Kennard, you will testify and your associate is here as counsel or——

Ms. **Howard**. I will also be sworn in as a witness.

Chairman **Wyden**. OK, why do you not identify yourself for the record, if you would?

Ms. **Howard**. Lauren Howard with Collier, Shannon, Reel and Scott, counsel to the National Cosmetology Association.

Chairman **Wyden**. All right; we cannot have you as both counsel and as a witness.

Ms. **Howard**. I understand that.

Chairman **Wyden**. Do you desire to be a witness then?

Ms. **Howard**. I will be a witness.

Chairman **Wyden**. All right; very good.

Please rise and raise your right hands.

[Witnesses sworn.]

Chairman **Wyden**. Thank you both. Again, we will make your prepared remarks part of the record. I hope I am pronouncing your name right, Ms. Kennard. Is it Cis Stock?

Ms. **Kennard**. Cis is my first name, Stock is my middle name, and Kennard is my last name.

Chairman **Wyden**. All right, Ms. Kennard, we welcome you and will make your remarks part of the record.

## TESTIMONY OF CIS STOCK KENNARD, LEGISLATIVE CHAIRMAN, NATIONAL COSMETOLOGY ASSOCIATION, WASHINGTON, DC; ACCOMPANIED BY LAUREN HOWARD, COLLIER, SHANNON, RILL AND SCOTT, COUNSEL TO NATIONAL COSMETOLOGY ASSOCIATION

Ms. **Kennard**. Thank you, Mr. Chairman.

My name is Cis Stock Kennard, and I currently serve on the board of directors for the National Cosmetology Association. Recently, I have been appointed NCA's legislative chairman. I am accompanied today by NCA's general counsel, Lauren Howard.

NCA is a nonprofit association comprised of almost 50,000 cosmetology professionals as well as more than 1,000 cosmetology schools located throughout the United States.

May I also offer my personal experience because I have been a licensed cosmetologist in the State of Washington for 17 years, a salon owner since 1978, and a school owner since 1985.

NCA has always been deeply committed to the safety of the cosmetology professional as well as the salon customer. Since NCA's leadership is and has always been comprised of working cosmetologists, this interest is not merely academic. If there were a safety problem out there, we would be the first to see it and the first to do something about it. In fact, our association has not found a significant problem with cosmetic safety.

Cosmetic safety is clearly an issue of grave importance. To me, it is not some abstract concept worthy of platitudes. Rather, it is an intensely personal matter, because, as a practicing cosmetologist for 17 years, it is my health and my life at stake. It is, therefore, with careful and considerate thought that I express my firm belief—and that of my professional association—in the safety of the products that cosmetologists use on a daily basis.

That is not to say that no one has ever suffered an adverse reaction to a cosmetic product. Clearly, that is untrue. As with food allergies, some people due to their particular genetic makeup may be especially sensitive to specific products. Some may work in places which do not meet Federal or State health and safety requirements while others may simply ignore manufacturer instructions for proper use. However, NCA believes that existing Federal and State authority is sufficient to address any health risk for cosmetic products.

Despite our confidence in these procedures, we believe that every reasonable effort should be made to ensure that no person—cosmetologist or consumer—suffers any adverse consequences from the use of cosmetics. The National Cosmetology Association wishes to emphasize that it supports sound cosmetic safety research and strongly endorses the cosmetics industry's continuing efforts in this area. We also fully support the provision of ingredient information for professional products. Providing this information to cosmetologists will be yet another step in the protection of our workers and our customers.

In addition, we publicly declare NCA's commitment to work with the Cosmetic, Toiletry and Fragrance Association and other industry organizations to accomplish the three-point program outlined by CTFA earlier today:

One, provisions for ingredient information for professional products;

Two, review of State cosmetology and health regulatory authority; and,

Three, the creation of additional educational programs for cosmetologists.

NCA believes that this industry-wide effort will address the issues raised at these hearings and will be an effective way to meet the concerns of the subcommittee. NCA is proud to participate in this program and to further underwrite its commitment to cosmetic safety. Thank you.

Chairman WYDEN. Thank you very much.

Ms. Howard, please.

Ms. HOWARD. I do not have a statement.

Chairman WYDEN. Very good.

Ms. HOWARD. But I am available to answer questions.

Chairman WYDEN. OK, Ms. Kennard, has the National Cosmetology Association changed its position on this ingredient labeling issue as well?

It is my understanding that like ICMAD, you all in the past were opposed, quite opposed, to ingredient disclosure for all products sold for professional use in the beauty industry. But are you changing your position for the record here today?

Ms. KENNARD. The National Cosmetology Association is the largest organization representing the cosmetology industry, and that cosmetology industry also is small business, and our concerns are that burdensome regulation could have an adverse effect on our membership in the cosmetology industry.

Chairman WYDEN. I would like to know whether you are going to join with ICMAD and with the CTFA in supporting ingredient labeling for professional products. That is what ICMAD said for the record. That is what we heard from the cosmetic association as well this morning. Is your association going to be for that or are you going to consider it?

Ms. KENNARD. Mr. Chairman, I made that statement that, yes; we will.

Chairman WYDEN. You said that ingredient labeling was burdensome.

Ms. KENNARD. No; I said additional regulation would be. The volunteer system that CTFA has outlined today is very effective, and we support that.

Chairman WYDEN. Are all cosmetologists educated about all the major chemical ingredients used in cosmetics today and their potential toxicity?

Ms. KENNARD. Mr. Chairman, let me address that from my experiences, and, first of all, the subcommittee might need to understand that each State regulates cosmetology differently, and, so, they have different curriculums and resources. Basically, I think I can speak from my own personal experience in that I am a cosmetology instructor, and I work from the basic cosmetology text, and from that textbook, it does instruct cosmetologists in the very basics of cosmetic ingredients and shampoos, rinses, permanent waves, hair coloring.

Chairman **Wyden**. But you are a leader in the field, and what I wanted to know was about the status of professionals in the field. Are all cosmetologists educated about the major different chemical ingredients used in cosmetics today and their potential toxicity?

Ms. **Kennard**. Mr. Wyden, it has been my experience being out in the workforce and knowing that the industry bases most of their work out of the standard textbook, I would have to answer that question that to the best of my knowledge, yes.

Ms. **Howard**. I would also like to say, Mr. Chairman, that the association has committed today to review educational programs and to ensure that cosmetologists are getting this information. So, to the extent it may not be done—and we are not saying that it is not being done—but we will be reviewing those programs and working with other industry associations to ensure that information gets to the working cosmetologist.

Chairman **Wyden**. How many of the States have programs at this point that you consider satisfactory?

The reason I ask the question is that I think it is a very first step. As I indicated today, what is being done in terms of the review programs at the State level, but over the years, there has been so much emphasis placed on voluntary action and the State programs. I would like to know at this point what you think of the State programs in this area. Are most of them satisfactory in your opinion?

Ms. **Kennard**. As part of my work as the legislative chairman, which I have had that appointment all of about 3 months and have served on the committee previously, we do review the State statutes, and I think that the commitment that we are making today is to further review them with more concentration on education toward cosmetics.

Chairman **Wyden**. From our understanding, certain kinds of cosmetic ingredients and underlying properties in them raise concerns about whether these issues come up in the education of someone who is a member of the Cosmetology Association.

Do you all personally get information about such things as phenol and phthalic acid? Are you familiar with those chemicals?

Ms. **Kennard**. Yes; you mean as a practicing cosmetologist?

Chairman **Wyden**. Yes; sure.

Ms. **Kennard**. The information that you are asking me, which I receive, are you talking about the technical breakdown of those products or the concerns and warnings about those products?

Chairman **Wyden**. It is an ingredient, and I am interested in knowing whether you as a leader in the field are familiar with the kind of thing it does.

Ms. **Kennard**. OK, as a practicing cosmetologist, my source of information regarding that would consist of, if it were contained within a product I was using and it was to be a concern, it would have a warning on it and/or I would be able to refer to my material safety data sheets and have information there, which would also be labeled within my own work area according to the OSHA requirements.

Chairman **Wyden**. These are ingredients that have been reported to produce skin and eye irritations, mutagenic effects, acute toxicity. All of them are reproductive toxins, and based on what you said to me today, my impression is that you did not walk in here knowing a great deal about these ingredients, is that correct?

Ms. **Kennard**. Mr. Chairman, I am a practicing cosmetologist, and——

Ms. **Howard**. I am sorry. Go ahead.

Ms. **Kennard**. Go ahead.

Ms. **Howard**. As Ms. Kennard stated, if there is an ingredient that is hazardous, she will be receiving information advising her of this through the MSDS Program, and it will tell her how to avoid any adverse effects.

Chairman **Wyden**. I know that program went into effect a month ago, but the information that we have gotten links these particular chemicals to some serious health effects, and if the information was getting out and had been made available, it would seem to me that particularly a leader in the field might have some knowledge about it. But we will want to follow up on this more in the days ahead.

Ms. Kennard, do you think the incidents we heard about in July were isolated kinds of situations—anything other than a very rare kind of occurrence?

Ms. **Kennard**. I have only read the testimony from those particular incidents, and I do not claim to be a doctor, but when I consider them in my own personal experience, yes; I believe that they are very isolated.

I work every day and have for 17 years, 8 to 12 hours a day in the industry, have exposure in a year's time to 60 people maybe on a daily basis, and I have not seen situations like this.

Chairman **Wyden**. So, you have not heard of any other accidents besides the ones that we discussed at our hearing in all your years in the industry?

Ms. **Kennard**. Any other accidents that relate to products? No; I have not.

Chairman **Wyden**. We have also heard that salon products are different than those normally sold to the public in that they may work faster and are more concentrated. Is this an argument in your view for labeling of salon products?

Ms. **Kennard**. Basically, according to FDA regulation, as much as I would know it, whether they are professional products or retail products, they all go through the same standards, and my concern, which you have brought to a lot of people's attention, if you are going to consider the working cosmetologist's health, I think that having the ingredients available and, as in our OSHA requirements, yes; that would be a problem.

Chairman **Wyden**. But you do not consider it burdensome at this point to require that the ingredients be clearly labeled on cosmetic products used in salons?

Ms. HOWARD. As we indicated in our testimony, we support the provision of ingredient information to professional cosmetologists.

Chairman WYDEN. That is different than labeling. I mean, what you are talking about, unless we are very clear on it, is a much more indirect process where people can get a warning and then go scurrying around trying to find other information.

What I would like to know for the record is whether your association will support clear ingredient labeling on the bottles or the cartons. Then if one looks at that, that will lay out what these ingredients are in salon products.

I am still unclear as to whether the association is going to support that.

Ms. HOWARD. We do not think that the information has to be on the label to be made available to the cosmetologist and to be useful to the cosmetologist.

Chairman WYDEN. We have also gotten information from OSHA that the MSDS has not always gotten down to the cosmetologist. I would hope that you all would support the position that the previous panel did, and I quote from there, "That ICMAD supports the use of ingredient disclosure for all products sold for professional use in the beauty industry."

I hope that that will mean labeling clearly on the bottles and not have people having to scurry around and try to figure out what technical language means by consulting something else. We will leave the record open if there is anything else that you all would like to add.

Ms. KENNARD. Thank you very much.

Ms. HOWARD. Thank you.

Chairman WYDEN. Thank you. Before we finish up, we have a number of things that we need to put into the record. A letter from Mr. John Paul Jones of John Paul Mitchell Systems recommending cosmetics manufacturers stop testing on animals. A letter from United Food and Commercial Workers. A NIOSH report.

Also, my colleague from Tennessee, a member of the subcommittee, Mr. Jim Cooper, has special interests and concerns in this area, and we are going to hold the record open for his remarks.

The Chair wants to make just one last point. We noted that CTFA had testified for the record that neither it nor any of its members had refused FDA requests for product substantiation data.

I have received a GAO report, the 1978 report, that indicates that FDA has been denied access to manufacturers' records. I am going to read a portion of this:

> Although the Federal Food, Drug, and Cosmetic Act authorizes FDA inspection of cosmetic manufacturer plants, it doesn't require manufacturers to permit FDA inspectors to examine their consumer complaint files, safety data, formulation data, shipping records, or other manufacturing records. As a result, manufacturers frequently refuse FDA access to such records. In some cases, FDA inspectors were even refused access to the plants. The following table summarizes the types and numbers of refusals that occurred between fiscal years 1968 and 1976.

Obviously, that is information of a period—a decade ago, 1968 to 1976, but it certainly is further evidence supporting the position of Dr. Young that data has been refused in the past.

Mr. **Hutt**. Mr. Wyden, could I provide additional information on that or would you prefer that we respond to it?

Chairman **Wyden**. This is very unorthodox.

Mr. **Hutt**. I understand that.

Chairman **Wyden**. We have already indicated that we are going to hold the record open for additional information, and the subcommittee is adjourned.

[Whereupon, at 3:50 p.m., the subcommittee was adjourned, subject to the call of the Chair.]

# APPENDIX

Third District, Oregon

News from
Congressman Ron Wyden

1406 Longworth House Office Building Washington, D.C. 20515 (202) 225-4811

## OPENING STATEMENT OF CONGRESSMAN RON WYDEN (D-OR) AT A HEARING ON COSMETICS HEALTH AND SAFETY ISSUES BEFORE THE SMALL BUSINESS SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

JULY 14, 1988

Today the Subcommittee begins a series of hearings to examine health and safety questions posed by the $17 billion U.S. cosmetics industry.

An enormous number of Americans are exposed to cosmetics every day. Increasing evidence suggests that some of these common products and their ingredients pose serious health hazards. Yet few, if any, chemicals have ever been banned as cosmetic ingredients.

Thousands of small businesses across this country -- beauty salons, barber shops, small retail stores and beauty schools -- are selling and using countless cosmetic products. Just like millions of cosmetic users and workers in this field, these small businesses are relying on the government to insure their safety and effectiveness.

Contrary to popular belief, the federal Food and Drug Administration (FDA) does not test cosmetics for safety, as it does foods and drugs. The FDA does not have the authority to require that manufacturers prove the safety of products before they are marketed. Amazingly, there are only two actions the federal Food and Drug Administration can do to protect consumers -- seize an occasionally contaminated batch of products and ask manufacturers to change their advertising claims.

Even if the agency suspects that serious adverse health effects are caused by a cosmetic product, the agency cannot ask for ingredient information from the manufacturer or require that the manufacturer provide test data to prove the product's safety or efficacy. In short, the burden of proof lies on the government's shoulders despite the fact that vital information about these potentially dangerous products is withheld from regulators. These regulatory gaps raise serious questions about the Food and Drug Administration's ability to effectively oversee this booming industry.

The FDA has told the Subcommittee staff that nearly 4,000 different chemicals are used in cosmetics, and another 4,000 in fragrances. These are mixed to form up to 40,000 combinations used in countless numbers of products. Cosmetic manufacturers aggressively market products containing chemicals that could cause cancer, birth defects, central nervous system disorders, skin and eye irritations, allergic reactions and other acute toxic effects.

Information provided by the Consumer Product Safety Commission and analyzed by the Subcommittee shows that hospital emergency rooms reported treating 47,000 cosmetic-induced injuries during 1987 alone. Over 151,000 injuries occurred between 1985 and 1987 -- resulting in 2,300 hospitalizations. Unnervingly, these injuries were caused by the whole range of cosmetic products -- soaps, nail preparations, hair "perms," hair straighteners, shampoos and dyes, creams, lotions, and facial masks.

Recently, many manufacturers have expanded into "fountain of youth" products which claim to "speed up the cell renewal process," repair skin, and make wrinkles fade or "lift upward." Notwithstanding the adage about beauty being only skin deep, the efficacy of such miraculous products would require active ingredients working well below the skin's surface. "Speed[ing] up the cell renewal process" implies a product containing far more than a little pigment and some moisturizer.

(more)

Federal law, incidentally, requires products "affect[ing] the structure or functions of the human body" to be regulated as drugs -- and undergo strict pre-market approval to assure their safety and efficacy. But to date, the FDA has not tested one of these products to safeguard consumers. It has only instructed companies to scale back their claims about the products -- and has operated under the assumption that the products don't cause harm. Unfortunately, no one -- neither the government nor the industry itself -- knows what risks or adverse health effects long-term exposure to cosmetics ingredients may cause.

Today we will hear from witnesses who have discovered how dangerous these products can be. An Oregonian will tell us about how her work with beauty parlor chemicals resulted in chronic asthma. An attorney will describe how hair straightener ignited his client's tresses. A physician and his patient will discuss neurologic damage attributed to the hair spray used on wigs.

In addition, Dr. Gary Grove will present his research on "anti-aging" creams. He will question whether these so-called cosmetics aren't, in fact, drugs -- with all the potential side-effects that can accompany drug use. And he will testify about the similarities between many of these over-the-counter products and Retin-A, a drug that the FDA has warned physicians to use with care, and Accutane, a drug known to cause birth defects.

Finally, Beth Shulman of the United Food and Commercial Workers union will tell us of the occupational health and safety concerns she constantly hears voiced by workers around the country. Not only do beauticians and industry workers face potential ill-effects, they have little or no access to information about which products are the most hazardous, and how to minimize contact with them.

As "baby boomers" age, we can expect the cosmetics industry -- particularly "fountain of youth" products -- to expand tremendously. The trend is clear: in the past decade, beauty product sales have increased one hundred percent. I think it is enormously important that we understand the health and safety consequences of the regulatory vacuum in which this huge and growing industry exists. That is the point of our Subcommittee's inquiry.

It is fitting that we begin today by hearing from some people whose lives have been irrevocably changed by their contact with everyday products that we -- apparently mistakenly -- assume must be harmless.

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## STATEMENT OF BETH SHULMAN
INTERNATIONAL VICE PRESIDENT
UNITED FOOD AND COMMERCIAL WORKERS INTERNATIONAL UNION
BEFORE THE SUBCOMMITTEE ON REGULATION
AND BUSINESS OPPORTUNITIES
JULY 14, 1988

Mr. Chairman and distinguished members of the Committee, my name is Beth Shulman and I am Vice President and Director of the Professional Hair Care & Beauty Trades Division of the United Food and Commercial Workers International Union, representing over 1.3-million workers organized in over 600 local unions throughout the United States and Canada, including over 40,000 workers in the hair care and beauty trades.

The task before this Committee -- to determine if the American public is being protected from hazardous chemicals found in cosmetics -- is an urgent one. I want to thank you for the opportunity to testify before your Committee on the serious health consequences of a government policy that permits cosmetic products to be sold and used by millions of consumers and workers with virtually no government oversight into the contents, effectiveness, or safety of these products.

As Director of the Professional Hair Care & Beauty Trades Division, I have spent the last few years crisscrossing the country listening and learning from our members. I have visited scores of salons, beauty schools, and hair shows -- and I can tell you without reservation this is an issue of genuine concern among our members.

There are now thousands of cosmetic products on the market today, used daily by millions of men and women -- and on a more continual basis by the thousands of Professional Hair Care & Beauty workers. These products may seem benign because of their attractive packaging and fragrances, but the chemical ingredients in them are not. These chemicals are causing serious health problems in the form of asthma, skin diseases, and neurological damage. Additionally, the long-term effects of these chemicals, in terms of cancer, reproductive disorders, and other long-term debilitating illnesses, are also being questioned. Our files are replete with letters from our members detailing illnesses and suffering caused by these supposedly safe cosmetic ingredients. The stories range from a hairdresser in Reese, Michigan who suffers from skin disease and upper respiratory infections since becoming a cosmetologist, to a hairdresser in Fair Lawn, New Jersey who was forced to retire at age 29 from the cosmetology business because of severe headaches and upper respiratory problems, to a salon in Kentucky where four out of the five hairdressers have suffered miscarriages, several of them multiple miscarriages, to reports recently published in a study by researchers from the University of California of headaches, nausea, and respiratory disturbances among cosmetologists applying the sculptured acrylic nails from popular in New York to Los Angeles. Because few of the products these professionals use are labeled with ingredients -- a situation that is neither illegal nor unusual -- they had no idea of the specific chemical they were using. Nor did they have any idea that the chemicals in these products might have a detrimental effect on their health.

Our position is not that cosmetic chemicals are so unsafe that they should be banned, but that the public and the workers using these products should not be human guinea pigs. There must be a policy in which the consumer and worker do not have to suffer severe health problems in order for the government to act. The American public has the right to be secure in the knowledge that when they purchase a product off a store shelf, or use it in a salon, that the products they are using are safe before it is put on the marketplace or on their bodies.

Most consumers as well as professionals would be surprised to learn that there is no regulation to assure the safety of cosmetics before they appear on store shelves or for use by hair care professionals. The government has no authority to require cosmetic manufacturers to test their products for safety -- or for effectiveness -- before they are used in salons or elsewhere. In addition, the Food and Drug Administration has no authority to require that cosmetic manufacturers provide any information to the FDA, thereby enabling them to conduct their own tests. The FDA cannot require a cosmetic manufacturer to supply such basic things as ingredient lists, consumer complaints, or test data -- making it almost impossible for the government to determine what chemicals are in cosmetic products, what cosmetics are causing health problems for consumers or workers, or whether they do what the label states. The cosmetic manufacturer is not even required to inform the FDA that a product or even the manufacturer exists.

To add insult to injury, no cosmetic product used in the salon or barber shop is required to have ingredient labeling. Even if a worker in a salon or barber shop wanted to avoid using hazardous chemicals in certain products, they would have no way of knowing what chemicals are contained in the products they use. If the manufacturer sells the same product to a consumer, they must provide the labeling of the ingredients but not so for the product used only for professionals. The result is the majority of products used by professionals bear no ingredient labels. Accordingly, hair care professionals cannot protect themselves or their customers before or after the use of a product, because they don't know what is in the product they are using. Thus, the average consumer runs a greater risk going to the hairdresser than buying a cosmetic off the shelf.

The statutes covering cosmetics, for the most part, were written over 50 years ago -- a time when scientists were largely unaware that the skin provided an easy route of chemicals into the bloodstream or that chemicals could enter the body through inhalation. Since then, thousands of manmade chemicals entered the marketplace. To a large degree, consumers and workers were the guinea pigs for testing the health effects of these products. We now know that many cause serious neurological damage, respiratory problems, and even cancer.

These very same chemicals are contained in thousands of cosmetics. The bottom line is that cosmetic products are mixtures of chemicals -- many which have been linked to serious health problems. Chemicals like formaldehyde, methylene chloride, ethyl methacrylate -- these highly toxic chemicals are found in a myriad of cosmetic products from hair sprays to sculptured nail applications. Formaldehyde is a serious irritant and is suspected of causing cancer; methylene chloride is a known neurotoxin and suspected of causing cancer; ethyl methacrylate causes severe allergic reactions and is suspected of causing nerve damage. In the late 1970's, the GAO compared a list of cosmetic ingredients with the government's own list of toxic substances and the results were compelling; more than 100 cosmetic ingredients were directly linked or suspected of being carcinogens; 24 more were suspected of causing birth defects; and scores more were known nervous system toxins.

Then there are the numerous studies indicating that workers in the barber and beauty trades may be at a higher risk than the general population for certain health problems ranging from cancer to dermatitis because they are exposed to a variety of toxic chemicals for longer periods. Underscoring the significance of these studies is the government's own estimates that one in 100 hairdressers will die of cancer from continued use of aerosol hair sprays that contain methylene chloride. The workers using these chemicals on a daily basis are clearly on the frontline confronting potential health hazards of major proportion.

More commonly known than the chemicals causing long-term problems are the many cosmetic products that cause acute reactions such as serious skin disorders, allergic reactions, and other short-term health effects. Among our own membership, there are reports of workers having to leave the hair care profession because of allergic reactions; the reports of consumers suffering allergic reactions, burns, and serious skin rashes from the products are prevalent. Additionally, the Consumer Product Safety Commission reports that 47,000 people were sent to the hospital in 1987 from injuries from cosmetic problems.

Despite our changing understanding over the past 50 years of the harmful impact of these cosmetic chemicals on workers in the beauty trades and consumers, there has been no change in government regulation of cosmetics. Moreover, the professional hair care worker is minimally, if ever, educated as to problems that the ingredients in cosmetics cause. They are not educated in the schools they go to because the curriculum does not require they be taught about the health hazards from the chemicals in cosmetics, and they are not warned by the manufacturers of the products that form the tools of their trade.

How are the 750,000 professional cosmetologists to determine the proper precautions to prevent hazardous exposures if they have no clue as to what is in their products, how to use them, or if they are safe? This is not only a dangerous situation for workers, but also for consumers, for professionals have no way to make certain that customers who have allergic reactions to specific chemicals are not exposed to those chemicals. Even more, if a consumer or worker suffers a reaction and, as is often the case, needs emergency medical treatment -- proper care must be delayed until the manufacturer is called and the specific ingredients are developed.

The lack of ingredient labeling, the FDA's lack of authority in terms of testing, submission of consumer complaints, company data and ingredient lists, however, are not the only glaring regulatory omissions. The FDA spends less on cosmetic regulation than it does for any other program. Even with what limited authority they have -- such as seizing dangerous products or contaminated products -- the FDA is too underfunded and unenthused to perform its duties effectively. For example, two years have passed, and still the FDA has yet to act on regulating the use of the highly toxic methylene chloride, despite its own alarming findings that its use in hair sprays dramatically increases the cancer risk facing cosmetologists. Ten years ago, the FDA banned the use of the neurotoxin methyl methacrylate for use in sculptured nail applications. Despite the ban, this chemical is still widely used. The FDA has done little to rid the industry of this proven neurotoxin. With a total number of less than 50 employees, out of the almost 7,000 for all of FDA, it is clear that oversight of the over $17-billion annual cosmetic industry is not a high priority.

We do not doubt industry claims that they not only conduct pre-market safety tests, but are genuinely concerned about the safety of their products. What concerns us is that the FDA cannot conduct its own independent evaluation prior to a product being marketed. Nor can they enforce safety measures for the industry -- such as limiting the amounts of certain known toxins in a product. Unlike all other products governed by the FDA -- drugs, medical devices, food additives -- the FDA cannot substantiate the safety of a cosmetic product prior to its entry into the marketplace. They can only react after the fact, when (as in the case of methylene chloride) an outside agency or party brings to their attention the fact that American consumers and workers may be in jeopardy. The FDA cannot protect the public by preventing dangerous exposure in the first instance.

A first step that would go a long way to correcting this situation, would be for Congress to pass legislation requiring that all cosmetic products -- whether sold to consumers or workers -- contain ingredient labels.

Second, more studies must be done in this $17-billion a year industry which has close to one-million workers who are approximately 90% female between the ages of 19 and 25 -- workers who are just beginning their working lives and who are most susceptible to reproductive hazards.

And last, there is clearly a need for additional FDA oversight into cosmetic safety. As Vice President of the UFCW and Director of the Professional Hair Care & Beauty Trades Division, I have gone to every state in the country to investigate the hazards and problems in this industry. What I hear time and time again is the high incidence of miscarriage, the high incidence of asthma or nervous disorders, and the increasingly high occurrence of skin diseases. While industry will argue that it is self-regulated and that they do tests on their products, obviously this does not guarantee the kind of independent testing we require of other products under the FDA's jurisdiction. We are talking about an industry that does not have to provide test data, consumer complaints, or a list of product ingredients to the government. How do we know that tests for the long-term effects of these chemicals have been done? Or that testing based on exposure in a salon has been done? We cannot have prevention unless we take control of these hazardous chemicals in the beauty industry both to protect the workers and the millions of consumers using these products.

The UFCW -- a worker organization -- has a strong track record when it comes to the safety of our members. Seven years ago our hair care members became concerned with the mandatory use of formaldehyde -- a severe irritant and suspected human carcinogen -- based sterilizers in salons. We arranged for a salon to be studied by public health agencies for exposure to formaldehyde -- and the results were alarming -- the study revealed dangerous concentrations of formaldehyde in the air when the product was used. Within weeks, we had petitioned all 50 states to review the requirement for formaldehyde based sterilizers -- and recommended safer alternatives. As a result of UFCW concern, 22 states banned or recommended against the use of formaldehyde within six months.

For over a decade, the UFCW has worked hard to gain protection for our professional hair care members. That is why we are here today. We urge this Subcommittee not to let the problems you will hear about today fade away, but to take quick action to protect the millions of consumers and workers who use cosmetic products.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Washington DC 20204

Richard A. Plumb
International Vice President
Director, Barbers and Cosmetologists Division
United Food & Commercial Workers
International Union, AFL-CIO & CLC
1775 K Street, N.W.
Washington, D.C. 20006

Dear Mr. Plumb:

This replies to your letter dated December 4, 1985, in which you asked six questions concerning our statutory authority for regulating cosmetic products.

In response to the specific questions you have raised, the answer to each is "no". We refer you to the enclosed reprint "Requirements of Laws and Regulations Enforced by the U.S. Food and Drug Administration" which provides a complete description of our regulatory authority with regard to cosmetics. Additionally, the following may provide you with the clarification you seek.

1. The Federal Food, Drug, and Cosmetic Act (FD&C Act), the statute under which we regulate cosmetics, prohibits the introduction into interstate commerce of products that are harmful to consumers or that are not truthfully labeled. Although the manufacturer is responsible for assuring the safety of cosmetic products, the FD&C Act does not specifically require safety testing of cosmetic products or their ingredients. It also does not require submission of data to us when safety testing is voluntarily carried out.

2. We do not have the statutory authority to require cosmetic manufacturers to submit a list of all ingredients used in their products. We have a voluntary registration program where manufacturers may, if they wish, file product formulations with us. Under the statutory authority of the Fair Packaging and Labeling Act (FPLA), all cosmetic products offered for sale as consumer commodities (i.e. sale to consumers at retail), are required to bear a list of ingredients on the package labels. Professional use products (e.g. those used solely by beauticians in beauty salons) are not required to bear ingredient declarations, since such products are not consumer commodities subject to the provisions of the FPLA.

3. We do not have the statutory authority under the laws that we enforce to require manufacturers to notify us when a new cosmetic product is placed on the market. Some information on marketed cosmetic products is obtained from voluntary registration of cosmetic formulations, periodic unannounced inspections of manufacturing establishments, and consumer and trade complaints about new products.

4. We do not have the statutory authority to pursue regulatory sanctions against coal-tar hair dyes that are harmful if the label of the hair dye product bears the following legend conspicuously displayed thereon:

"Caution - This product contains ingredients which may cause skin irritation on certain individuals and a preliminary test according to accompanying directions should first be made. This product must not be used for dyeing the eyelashes or eyebrows; to do so may cause blindness.", and the labeling bears adequate directions for such preliminary testing.

Coal-tar hair dye products not bearing the above caution statement are not subject to the Section 601(a) exemption.

5 and 6. We do not have statutory authority to require manufacturers to submit a list of all ingredients (or their quantities) to us. Consequently, we do not have a specific list of all cosmetic products containing methylene chloride or information as to how much of a particular chemical (e.g. formaldehyde) may be found in all cosmetic products. However, we do have semi-quantitative information on ingredients of products voluntarily registered with us. With respect to formaldehyde in particular, we have a good understanding of its usage concentrations in cosmetics.

We hope that this answers your questions.

Since you did mention methylene chloride in your letter, we have also enclosed a copy of the December 18, 1985 Federal Register proposed rule which would ban the use of methylene chloride as an ingredient of aerosol cosmetic products. In the spirit of this Federal Register proposal, you can be assured that we will continue to keep abreast of safety issues in the cosmetics area.

Sincerely yours,

John M. Taylor
Director
Office of Compliance
Center for Food Safety
and Applied Nutrition

Enclosures:
as stated above

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# Testimony
# of
# Kristie Smith
# Before the
# Subcommittee on Regulation and Business Opportunities
# July 14, 1988

My name is Kristie Smith. I am 24 years old.

Four years ago, in September, of 1984, I enrolled in a local beauty college. The school was to last one year, but I only made it part way through.

For shortly after I enrolled in beauty school, I began to have trouble breathing. I didn't think much of it at first, but as the months went by, things began to get worse and worse.

In beauty school you spend much of the time actually cutting and setting hair or applying perm and other hair products to patrons that come into the school. In fact, after only a few months of instruction, you pretty much spend full time working on patrons.

During this time, when I was working around all these beauty products my breathing got real bad. There would be times when I was in school that my chest got so tight I couldn't catch my breath, and I would turn purple and have to leave the room. It felt like I was under water.

The terrible thing is, it didn't go away when I got home. After a day in the school working on patrons' hair, I would be up all night trying to catch my breath.

Eight months after I started the school I went to the emergency room because I couldn't breathe.

But things kept getting worse, and the episodes of feeling like I was under water occurred more and more frequently at the school. The management of the school frowned on me leaving the room so often; and their response to my lack of breath was: stop complaining.

Then, in June, ten months after I started beauty college, I went to a doctor. I was diagnosed with occupational asthma and told it was from exposure to the chemicals I was using at the school. The doctors told me to take a leave of absence from the school and eventually told me never to go back.

In January, 1987, I went to see another specialist who confirmed that I have occupational asthma -- an irreversible condition.

It's been almost three years' time that I'm living with this lung condition. The worst part is the attacks, which, as the last one did, last as long as a month, in which just simple things like catching my breath become almost impossible. For some reason, my problem gets worse at night. During the attacks I sit up all night trying to breathe. The doctors have given me medication to help alleviate some of the pain, but they are powerful drugs that make my nose and throat numb.

Going out is often risky for me because my lungs are sensitive. Whereas before I attended beauty school I could go to the theater or store with no concern, now a whiff of perfume can set off an attack.

And when the attacks come it can take me up to ten tries to catch my breath each time. When I do, I just laugh -- it's the best feeling to just breathe even once.

I'm 24 and the one career I was planning for is now out of my reach. I have permanent asthma.

I have sued and settled with the beauty school that I attended. But what happened to me could happen to anyone walking into this or any other school or salon. Or it could happen to a customer.

There was absolutely no ventilation in the room where we worked on customers except the front door. But no one told us that may be a problem. No one told us about any problems from breathing in all these fumes.

In fact, when I left the school after ten months because I couldn't breathe, they sued me for not paying for the last two months I did not attend. My career plans were totally ruined, but it never occurred to them that they had a responsibility.

I am shocked to learn that the products I used were not approved by some agency. I know nothing I worked with was labeled -- and it took my lawyers a long time to figure out the ingredients.

What I am realy angry about is that no one told me -- or anyone else in my school -- that the chemicals we were using might be dangerous. It's not right that the government doesn't require this information to be passed on. It is especially not right that I had no idea what was in the products I worked with. Unless this is all changed, more and more people will get hurt.

**Testimony**
**of**
**Edith Khatami**
**Before the**
**Subcommittee on Regulation and**
**Business Opportunities**
**July 14, 1988**

Good morning, my name is Edith Khatami. I immigrated to the United States in 1972 from Vienna, Austria with my two children. In 1981, when my children were older, I began to look for work and, because of my background as a cosmetologist in Europe, I answered an ad by Loral Wigs & Boutique Shop looking for stylists in Cupertino, California. I was hired and began work at Loral in 1982.

My job consisted of servicing wigs -- including cutting, styling, washing of both human and synthetic wigs, and selling these wigs to the public. My wigs were bought by cancer patients from Stanford Hospital, who came to me to do wigs for them.

Before I started my work for Loral I was very healthy and had no problems whatsoever.

There was a small back room in which we did the wigs and in the front there were three chairs for ladies and one for men. I spent a lot of time working on the wigs in that small back room. In addition to cutting the wigs, we styled them by using hair sprays called Streaks 'n Tips and La Charme which I am told contains methylene chloride, the kind consumers use. The area in which we did the washing, cutting, conditioning, spraying, and styling of the wigs, was very poorly ventilated. There was no air conditioning to help circulate the air. We had our lunch in that same room during the day.

In 1984, two years after I began at Loral, I started to feel very nauseous, dizzy, and started having vision problems. My coworker, Carol Guerrero had some of the exact same symptoms. She felt very nauseous, dizzy, and, in fact, she said she couldn't wait on customers any more because she had become disoriented and had trouble counting money. Both myself and Carol had chest pains and the feeling like we couldn't breathe. There was numbness and tingling in our extremities as well.

What finally made us alarmed about our health was that Carol fell outside the shop. She was feeling incredibly confused and disoriented when it happened. We decided to see a doctor. And we both asked what happened to us in this little shop. We were healthy and now we are not. I got referred to Stanford Hospital and then to the Santa Clara Valley Medical Center and then to Dr. Jim Cone. They diagnosed me as having a central nervous system disorder called cognitive disfunction and also occupational asthma caused by the methylene chloride in the cosmetics I was using. But nobody told me and nobody warned me or instructed me concerning the products we were using.

In October, 1985 I left my job and I haven't been able to work since then. Part of the problem being now that I can't remember things that I did just a short while ago. That's one of the health effects of the neurotoxins I was exposed to. I have to write everything down. How can I go to an employer and ask him to hire me when I don't have any memory. But I'm the lucky one -- my friend Carol can barely do the most easy tasks. Because she has barely any memory function, she needs help in her house. She can't cook because she forgets to turn off the oven. She often forgets if she has eaten.

And she, like me, has a cane because we have a hard time keeping our balance.

No one ever warned me that the chemicals I was using may be harmful to me and I can't believe the difference it has now made in my life. It has been really hard and the most horrible part of it all is that I know that I will always have this condition.

I know from going to stores that other hair sprays have methylene chloride. I was shocked to find out that over two years ago, the government proposed a ban on methylene chloride because it causes cancer but has never done anything about it.

How many more people have to get sick before the government does something about it? It's not fair. It's not right. If the government doesn't care, who will?

# TESTIMONY OF RONALD A. KARP

My name is Ronald A. Karp. I am a partner in the firm of Chaikin & Karp, P.C. located in Washington, D.C. [1232 17th St., N.W., Washington, D.C. 20036 (202) 659-8383] and Montgomery County, Maryland [Penthouse One, 51 Monroe Street, Rockville, Maryland 20850 (301) 424-7020].

I am a past president of the Trial Lawyers Association of Metropolitan Washington, D.C. and currently, the District of Columbia delegate to the American Trial Lawyers Association.

I recently had the opportunity of trying a case in the federal court in Baltimore, Maryland which resulted in a District of Columbia woman receiving a $450,000 jury verdict against a cosmetic company. That verdict has just been upheld by the United States Court of Appeals for the Fourth Circuit. [Laverne Greene v. M & M Products Company, No. 87-3725, decided July 1, 1988].

During the course of this litigation, and particularly after the verdict which was reported in the media and in legal journals, I began hearing from lawyers all over the country who had similar cases. Black women who are using hair products designed to give them the popular "jeri-curl" were having their hair catch on fire and suffering severe burns.

In my case, Laverne Greene, age 42, used the product on the evening of December 21, 1985, covered her head and went to sleep. The next morning she was alone, driving in a car when she struck a match to light a cigarette. A spark flew to her hair and she heard "popping and cracking" noises. Her head had become a human torch and she tried to pat out the fire which had now spread to the roof of her car. She got out of her car and two men, seeing her in distress, reached over and managed to eventually extinguish the flames. She was hospitalized for four weeks with severe burns. Her eyes were swollen shut and she underwent painful burn treatment, including skin grafts.

At first we were led to believe by the company that the incident was a fluke and that there was no relationship between the hair fire and the hair products. The Court ordered the company to produce complaints of prior incidents and I soon learned that the incident was not really a fluke at all. It had happended before.

We then had tests performed at the Worcester Polytech Institute in Massachusetts by Professor Richard Custer, who was formerly with the National Bureau of Standards and is a specialist in fire prevention.

Professor Custer reported to me that chemicals used in the hair products caused a "grease fire" to occur when they were ignited. Normal, untreated hair could be extinguished by patting it out if it should catch fire, but hair treated with the "jeri-curl" products cannot be readily extinguished. Indeed, when Laverne Greene tried to pat out the "grease fire" that was on her head, her hands became burned as well.

I have since heard from countless lawyers all over the country who have related to me tragic similar incidents caused by a variety of hair products, all marketed to predominately black females who want a "jeri-curl."

As we speak right now, I have no doubt that thousands, perhaps millions of women have these products on their hair without any understanding of the danger they may suffer if their hair comes into contact with a spark or any other source of ignition.

Some of these products carry a warning which states: "Keep Hair Away From Open Flames." We had a Human Factors expert testify at trial, one Dr. Robert Cunitz, also formerly employed by the National Bureau of Standards.

Dr. Cunitz testified that this kind of "warning" is wholly insufficient to adequately notify the consumer of the risks involved in using these hair products. He pointed out that the "warning" does not tell one how long one must stay away from open flames, or why one must stay away, or whether matches or smoking can cause a special hazard. He felt that the "warning" was not adequately displayed and fundamentally that the products were too dangerous to be on the market in their current state.

There are various companies that market "jeri-curl" products and some have no warnings at all! These products contain such chemicals as glycerine and propylene glycal, the residue of which causes the grease fire when ignited.

Women who are buying these products ought to be warned of the risks involved in using them so that they can make an informed choice. They ought to be explicitly told that smoking around these products can be more than hazardous to your health. When hair containing these products are ignited, one's life can change forever, because the scarring is permanent, the burns so deep that no new hair will grow, the sweat glands are destroyed so that going out in the sun is not an option anymore.

As I speak to you now, Laverne Greene is sitting inside her apartment. She cannot go out in the sun, even with her head covered, without experiencing pain. She cannot go to the supermarket without people starring at her head because the burns are over her ears and she must wear extensive covering to hide the burns. She is a prisoner in her own apartment as are many burn patients, but these burns could have been easily prevented.

I have been told of similar tragedies involving teenagers who use "jeri-curl" products. What will happen to their futures? All of this is too high a price to pay for inadequate warnings.

It seems to me that if we can force cigarette manufacturers to put warnings on cigarette packs that tell consumers they may get cancer in the future, we can force cosmetic manufacturers to warn women that their heads may turn into human torches tomorrow morning.

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Statement of

James E. Cone, MD, MPH

Chief, Occupational Health Clinic
San Francisco General Hospital

Before the

Subcommittee on Regulation and Business Opportunities

Small Business Committee
House of Representatives

July 14, 1988

# Occupational Hazards of Cosmetology

- by James E. Cone, MD, MPH
Chief, Occupational Health Clinic
San Francisco General Hospital

## I. Introduction

Mr. Chairman and Members of the Committee:

My name is James E. Cone. I am a medical doctor, and hold a Masters degree in Public Health. I am currently Chief of the Occupational Health Clinic of the University of California, located at San Francisco General Hospital. I currently hold the position of Assistant Clinical Professor in the Department of Medicine at the University of California, San Francisco.

The Occupational Health Clinic is a multidisciplinary training, service and research center which since 1979 has provided medical practicioners, industry, unions and governmental agencies with consultations regarding the effects of work and environmental exposures on health. We are one of an increasing number of referral centers located in academic medical centers around the country where clinicians in emergency rooms and medical practices may call and refer patients with especially puzzling or difficult cases. We thus see cases with potential public health implications, and combine a clinical practice based in internal medicine with a public health practice based on industrial hygiene, epidemiology and toxicology.

I am pleased to be here today to discuss four representative cases which I believe illustrate a problem facing a large number of cosmetologists and hairdressers as well as consumers: lack of awareness of the potential health hazards of cosmetics due to failure to warn on the part of the manufacturers.

## II. Case presentations from the Occupational Health Clinic of the University of California, at San Francisco General Hospital

### 1. Asthma

The first case is that of Ms. K, a 36 year old female cosmetologist who presented to the Occupational Health Clinic with asthma exacerbated by her work. She had a prior history of seasonal asthma since age 18, lasting 1 month each year in the spring only. She attended Beauty College and worked as a cosmetologist without significant problems until 1985.

She then began work in a large beauty salon inside a large department store. It was an enclosed shop, with six stylists. Ceiling vents were present but were inoperative. Hair dryers were vented to the salon room. This situation, with apparent lack of adequate ventilation, is all too common in beauty salons around the country which I have visited.

Several months after beginning work in this salon, Ms. K. began noting worsening of her asthma symptoms, with wheezing which progressed to the point she required frequent visits to the Emergency Department of a nearby hospital. She was treated with multiple asthma medications, including steroids.

Her symptoms continued to progress despite the medications. She consulted an allergy clinic where she was noted to have reversible changes on pulmonary function testing. Her symptoms would start at about 10 am, about 2 hours after starting work. Her symptoms were improved on weekends and vacations.

She finally consulted the Occupational Health Clinic when she began to suspect an occupational cause. She had never been told that many of the constituents of hair products were potential respiratory irritants or sensitizers. Our evaluation included a careful history of exposures, physical examination, pulmonary function testing, and a walk-through of the salon. Air filters were noted to be stopped-up by hair and debris.

Inadequate ventilation was noted. Labels were absent from many professional hair care and beauty products. Material safety data sheets where they were present indicated multiple trade secret products, and were not available at all for some products.

Due to the multiple potential irritant and allergenic exposures, with lack of information which would enable us to further narrow down what the potential causes of her asthma exacerbation might have been, we recommended removal from the workplace, and improvement in ventilation to prevent others from developing similar problems in the future. Her symptoms are now 75% improved since stopping work, and she is using only an inhaled medication occasionally, and has not required emergency department visits since stopping further exposure.

This case illustrates the common problem of exacerbation of an underlying condition due to exposure to products without adequate warning, in a poorly ventilated salon.

## 2. Contact dermatitis and contact urticaria syndrome with anaphylaxis

A 42 year old beautician consulted the Occupational Health Clinic with symptoms of fatigue, headaches, aching in her legs and nausea which were associated with work in a hair salon, cutting hair, applying permanent wave solutions, tints, bleaches and shampoos. In June 1986 she was stocking shelves in the salon storeroom with bottles, including a bottle of permanent wave solution in a box which had broken. She noted strong odors and immediate irritation from the solution. She reported immediate difficulty breathing, with overwhelming weakness. She fell off a stool onto the ground, and bruised her back and ankle. She went home with these symptoms, and then noted onset of urticaria or hives over her hands, arms and scalp.

She went to a local emergency room where she was told she had chemical urticaria and chemical poisoning and was told not to return to the jobsite. She was treated with antihistamines and steroids. She attempted to return to work but each time, on exposure to tints or permanent wave solutions she had to go to the emergency room with difficulty breathing and severe hives over her body. She required treatment with injected epinephrine on one occasion due to the potentially-life threatening nature of her symptoms of anaphylaxis due to contact urticaria syndrome. She was unable to provide us or any of the emergency physicians with the chemical constituents of the products she was exposed to due the lack of labels on the products.

Thus we were unable to advise her about which of the multiple specific chemicals might have been responsible for her reaction, and had to advise her that vocational rehabilitation to another occupation would most likely be necessary.

## 3. Upper Respiratory Irritation due to acrylics among Beauty School Students

We evaluated two students in the same Beauty School who had exposure to artificial nail products while in training. One student took the product home to practice on her own nails, and noted a bloody nose shortly after using the product over several hours, and for the following 24 hours intermittently. She had symptoms of headache, sorethroat, and fatigue. A baby in the home also had bloody nose, red throat, red eyes. Four other students also noted bloody noses and mouth sores following exposure.

They applied primer to nails, with brush from a bottle. They used a product containing acrylic ester monomers called "Magic Sculptura". They then placed form on the nails, and dipped the brush into a liquid catalyst (acrylic ester monomers, dimethyl d-toluidine, and BHT) and then added powder (polyethyl methacrylate and a peroxide) to form a liquid plastic. The final step was removal of the form and filing the nail. They worked in a large room with 100 other students without windows or artificial ventilation other than a fan at either end of the room. No gloves or respiratory protection were worn by the students.

The school was contacted. The owners reportedly contacted the manufacturer who requested that the product be returned to them. The school switched to a different nail product with reportedly reduced problems subsequently.

This case illustrates the hazards which may be faced in a training setting with products taken home to practice, and potential exposures to family members including small children, to potentially very toxic compounds.

While it was admirable that the company recalled the product at least from that school's supply, we wonder about all the other schools and salons who were also using the same batch of material and potentially suffering similar effects. Were their products recalled as well?

### 4. Chronic Toxic Encephalopathy due to Methylene chloride

The Occupational Health Clinic was referred two workers in a local wig salon with similar problems.

I will discuss one of the cases which illustrates the severe potentially disabling hazards of work in the hair care industry.

Ms G. is a 37 year old Hispanic female who was referred by her attorney for evaluation of symptoms of headaches, dizziness, slowed thinking, and episodes of feeling "blank and dumfounded" while at work in a small poorly ventilated room at a local Wig salon which supplies wigs to cancer chemotherapy patients. These problems progressively worsened in intensity and severity, to the point that one day she noted severe headache, felt "cloudy", and became dizzy, lost her balance and fell, injuring her knees and side of her head.

She went to the local hospital emergency room due to persistent symptoms, where she had a Computed Axial Tomogram of her head, electroencephalograms on two occasions and complete neurological workup which was negative for any structural abnormality except for nerve conduction abnormalities in the right wrist. She was unable to return to work due to persistent headache, numbness and tingling of her hands, "blank spells" and memory loss. She was subsequently referred to a local mental health center for depression and counselling. She was evaluated with neuropsychological testing which showed considerable cognitive impairment. She was referred for rehabilitation counselling, and finally to the occupational health clinic. She was found to have carpal tunnel syndrome most likely due to repetitive motion trauma from work as a wig stylist, with significant nerve damage in the right wrist.

On further neuropsychological testing, she was found to have psychomotor, memory, and sensory function deficits consistent with methylene chloride toxicity. Her depression was felt to be secondary to the functional losses she experienced as a result of her exposures.

She was exposed primarily to La Charme Wig Sheen and Conditioner which contained SD-Alcohol 40, Methylene Chloride, isobutane, mineral oil, propane, PPG-14, butyl ether and a fragrance. She also was exposed to Nestle Streaks and Tips, a temporary spray-on hair color. The ingredience of the "gold dazzle" color are isobutane, SD-Alcohol 40, Methylene chloide, propane, Brown's Powder, PVP-VA copolymer, isopropyl alcohol, dimethylphthalate and fragrance. Her work was performed in a 10X5 foot unventilated room. The room had reportedly a continuous odor of drying wigs throughout the day.

Methylene chloride is a major solvent used in paint removers, degreasers, and as an aerosolizing agent replacing fluorocarbons in aerosol sprays such as insecticides and hair sprays. It is also used as a blowing agent in the production of urethane foams, and as a solvent in the production of decaffeinated coffee. It is readily absorbed through the lungs, and metabolized in the liver to carbon monoxide. This metabolic product may interact with the solvent to produce lack of oxygen in the tissues, particularly the brain and heart. No large scale studies of the chronic brain effects of this substance in humans has been published, but loss of consciousness, confusion and death have been reported from occupational overexposure in unventilated settings. There have been case reports of dementia following methylene chloride exposure.

Partially as a result of these two cases of dementing illness in Wig workers exposed to methylene chloride we have seen, the Northern California Occupational Health Center is currently pursuing a research study funded by the National Institute of Environmental Health Sciences, of chronically-exposed airline strippers and painters to evaluate the potential for neuropsychological effects among such workers.

## III. Discussion

The problems faced by the cosmetologist in protecting themselves from potential hazards in their workplace are made significantly more difficult by the absence of effective information about the hazards, either during their training programs, or on the job. As the above cases illustrate, the hazards are such that the cosmetologist must ultimately choose between his or her health or the job. By the time the relationship between work and illnesses becomes obvious, continued work in the profession often becomes virtually impossible due to the extreme sensitivity or severe health effects which may be produced by many of the chemicals used.

1. The first step in solving these problems is providing essential information in an effective manner to those who work with such chemicals on a daily basis. Cosmetic Labeling of all professional as well as consumer products that explicitly outlines the potential hazards associated with the actual names of all ingredients is needed. To avoid overwhelming the label with information, readily identifiable symbols relating the specific organ or type of health problem associated with the specific chemicals involved might be useful to warn cosmetologists and others of potential hazards.

2. As important is a requirement that all schools of cosmetology and hairdressing provide adequate background in chemistry and toxicology to be able to understand the labels.Students should be trained sufficiently that they know the basics of industrial hygiene as applied to their industry so that they know what should be provided in terms of ventilation, skin protection and respiratory protection.

3. Most importantly, substitution of less hazardous ingredients and processes must be stressed. Ingredients which are known or suspected carcinogens must be banned, and strong irritants or sensitizers should be removed from products.

4. Premarket testing is needed, preferably by an impartial research institute not tied to the industry. Testing of ALL ingredients, not just new ones, is necessary.

5. Further studies of an epidemiologic type are needed to evaluate the frequency of acute and chronic health hazards to cosmetologists. These should include studies not just of mortality due to cancer, but also reproductive studies, and studies of asthma, dermatitis and multiple chemical sensitivities potentially produced by professional cosmetic products.

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# OPENING REMARKS

to

# THE SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

# COMMITTEE ON SMALL BUSINESS

# UNITED STATES HOUSE OF REPRESENTATIVES

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I am very pleased to participate in these hearings. Hopefully, I will be able to provide some insights that will allow your committee to be more informed on the important issues that you are concerned with.

I have been actively involved in skin care product development and claim substantiation research for approximately 15 years. Currently, I am the Vice President for Research and Development of K.G.L. Inc. and head their Skin Study Center outside Philadelphia. This is a privately owned, independent testing center that I am very proud to say has earned an international reputation for its innovative work in monitoring changes in skin structure and function non-invasively. We evaluate the safety and efficacy of topically applied products and our clientele is broad based and represents all aspects of the skin care industry and includes both cosmetic companies and pharmaceutical firms. We work strictly on a "fee for service" basis and as such do not endorse products or receive royalties from their sales. What's important to us is that we adequately judge whether a product is safe for its intended use and can perform as well as its manufacturer claims.

It is quite clear that the veracity and integrity of the skin care products industry is being brought into question by a number of groups. If anyone would have asked me 5 or 6 years ago " How much science is there behind the various claims being made for skin care products? ", I would have been the first to admit that there was a lot more science fiction than real science. However, this is clearly no longer the case. In fact the truly innovative research programs that are being conducted to study various aspects of normal human skin physiology and cutaneous aging are more than likely being funded by these commercial interests.

While there is no doubt that some truly outlandish claims are being made, for the most part, these are the handiwork of "here-today, gone tomorrow" companies. I feel that most of the established companies are going to great lengths to ensure that their products do indeed live up to their claims. This is not to say that their advertisements are based solely on the facts and contain no fiction. Some degree of "puffery" has always been tolerated and inadvertent misinterpretation of data do occur; however, it is highly unlikely that any reputable firm has intentionally lied in their advertising for the very simple reason that we now do have the capabilities to either confirm or deny these types of claims.

It should be appreciated that skin is highly complex in its function, composition and structure. Nevertheless, it has certain cosmetic defects such as being too dry, too rough, too greasy, too aged, etc. that can be recognized quite easily. By clearly defining these defects, we can create the necessary basis for developing scientific methods by which the degree of success of skin care products designed to alleviate these conditions can be measured. In actual practice this might not be as straight forward and easy to do as one would wish but such an approach has become an important part of successful product development and critical in creating competitive marketing strategies.

There is considerable consumer interest in products that deliver readily perceivable benefits that are the result of these scientific advances. Nevertheless, we must appreciate that consumers are highly susceptible to advertisements that claim product efficacy, especially if endorsed by celebrities even if they have no credentials in the cosmetic or skin care sciences. Otherwise reasonable adults can easily be misled into purchasing various products, devices and treatments that couldn't possibly live up to their claims of providing rejuvenation and eternal youthfulness. It is true that if false or greatly exaggerated claims are being made for a product the user will soon discover that it does not perform as promised and thus will not buy it again. This may be of no consequence to a company if their marketing group is interested in a successful launch instead of a successful product. However, over the long run such a strategy could prove disastrous. Indeed, the failure of a product to live up to its touted claims can have a ripple effect that makes potential customers skeptical of other offerings in that line if not the overall brand.

The recent introduction of a new class of "anti-aging" products that promised to retard or reverse the signs of aging has prompted the FDA to serve notice that many of these treatment claims fall under the drug definition of the law. Determining how far one may go before a performance claim will be deemed a therapeutic claim that subjects the product to regulation as a drug is certainly a critical issue. Whether the more then 50-year-old Food, Drug & Cosmetic Act needs to be revised to reflect the recent technological advances made in cosmetic and skin care science should be carefully considered. Obviously, if a manufacturer can formulate and distribute a cosmetic-drug product in accordance with a FDA monograph such as the Skin Protectant, Acne or Sunscreen monograph, I think they would be well advised to do so.

It is important to note that in this recent flurry of FDA activity, the safety of these products was not an issue. This is not surprising since most cosmetic companies do considerable pre-market testing to establish the safety of their newly created products. Indeed the industry should be praised for the approach it has taken to self-regulation since it works so well. A key ingredient in this success story is the C.T.F.A. (Cosmetic, Toiletries and Fragrance Association). This large group of manufacturers strongly urges that all companies actively participate in the voluntary reporting program being conducted by the FDA. The C.T.F.A. also has published "Technical Guidelines" that covers general concepts of what is entailed in adequately testing a product for safety.

The CTFA has also been instrumental in organizing the CIR (Cosmetic Ingredient Review). This consist of an independent panel of experts, toxicologists, dermatologists, formulators, etc. who are systematically and thoroughly evaluating cosmetic ingredients from a safety point of view. As you might well imagine this is an enormous undertaking. Priorities based on degree of use have been established and considerable progress has been made in going through the list with the information gathered being shared with all interested parties.

This doesn't mean that there isn't some room for improvement. For one thing the FDA is severely limited in both manpower and funding and if it is to remain an effective watch dog this must be remedied. I also feel that the potential for a safety problem to emerge is considerably greater with small businesses as they most likely do not have the resources to do adequate safety testing. I am especially concerned that some beauty shop operators, cosmetologists and estheticians are becoming more adventuresome in creating "home brewed remedies" for their local patrons. How they can be properly regulated without adversely effecting their businesses is not, at least to me, readily apparent.

It is certain that various consumer groups and regulatory agencies will continue to impose greater responsibilities on the manufacturers of cosmetics and skin care products to assure the safety and efficacy of newly marketed formulations. In light of this trend, I would strongly urge the manufacturers to undertake a voluntary effort to develop guidelines that define acceptable marketing and promotional practices as well as standardizing the methods and analytical techniques used to generate these performance claims. These "principles of conduct" guidelines should specifically advocate advertising claims that stress product performance claims that can be scientifically verified. They should also stress that all instrumental tests be relevant to the "real world" and always be supported by appropriately designed subjective assessments by non-biased panelists and expert graders. Clearly these guidelines must not condone advertisements that make unsubstantiated assertions that are designed to impress, bewilder and/or alarm the consumer.

# Cosmetic Product Claims

**"CHANEL LIFT SERUM ANTI-WRINKLE COMPLEX":** ". . . 45% wrinkle reduction, clinically proven. . . . a more youthful look without plastic surgery. . . . formulated to firm significantly, to maintain a younger look over time with regular use. . . . counteract the effects of . . . aging . . . **Evening out lines and wrinkles** as it exerts a gentle upward pressure from deep within skin. . . . Tiny molecules of Plastoderm penetrate quickly into various skin levels. . . . Molecules absorb . . . and expand, exerting upward pressure to 'lift' wrinkles upward. . . . natural proteins and energy-boosting nutrients is designed to traverse deep within the skin . . . as if skin were . . . 'lifted' from within. . . . formulated to help support the elemental tissue of the skin. . . ."

**"ESTEE LAUDER NIGHT REPAIR Cellular Recovery Complex"** . . . enhances the natural rate of repair of cells damaged by the ultraviolet light . . . contains a complex of natural ingredients that supplements your own skin's repair mechanisms . . . Laboratory tests show a 37–38% rate of increase in the natural repair of cells damaged. . . . Hyaluronic acid, a critical ingredient which helps bind moisture into your skin, is also damaged by ultra violet exposure. Night Repair replaces hyaluronic acid in its most functional form . . . penetrates completely . . . supplements your own mechanisms as they start to falter . . . helps control the signs of aging . . . beauty breakthrough that changed the science of **skin care** to **skin repair**. . . ."

**"ACTI-VITA ANTI-WRINKLE CONCENTRATE":** ". . . contains concentrated active ingredients: a multi-vitamin solution . . . a complex of proteins . . . and UVA-UVB sunfilters. . . . After three weeks' treatment, your skin is transformed, because of the active ingredients contained in the formula, which stimulate cell renewal. Your epidermis renews itself, becomes finer, smoother, regains youthful dynamism, freshness and energy. . . ."

**"MORNING RECOVERY SOLUTION":** ". . . When stress, late nights, that extra drink and even premenstrual tension make skin look dull and tired . . . you need the energizer that helps your skin keep up with your life style . . . MORNING RECOVERY SOLUTION. The energy boost you use in the morning. . . . works with your skin's natural micro-circulation process . . . it revives skin with an instant 'firming lift" . . . Contains ingredients that promote an increase in the amount of energy — producing oxygen available to skin cells . . ."

# Cosmetic Product Claims (Cont'd)

**''FD-29 COMPLETE ANTI-AGING COMPLEX'':** ". . . anti-aging cream formulated to work with — and augment — natural skin functions. Scientific tests prove . . . wrinkles will be measurably smoother and skin will be visibly younger looking within 21 days. . . . reduce years of lines and wrinkles. . . . New anti-aging discovery . . ."

**''NIGHTLY REQUIREMENT CREME'':** ". . . not just skin repair . . . promote brand new looking skin. . . . Strengthened by energizing ingredients that help supply skin cells with the oxygen necessary to help accelerate development and proliferation of skin cells. . . . Has a natural adhesive affinity for collagen, . . . nurturing biological extracts. . . ."

**''LANCOME NIOSOME Systeme Anti-Age Daytime Skin Treatment'':** ". . . mimics skin's cellular support structure . . . TARGETS anti-aging activities to where skin requires them . . . Anti-Aging System . . . recreate the structure of a young skin . . . a system of Niosomes$^{TM}$ — microscopic spheres which carry active, anti-aging ingredients into your skin . . . helps to rebuild the intercellular network of your skin . . . it recreates the conditions of younger skin."

Third District, Oregon

News from
Congressman Ron Wyden

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### OPENING STATEMENT OF
### CHAIRMAN RON WYDEN (D-OR)
### AT A HEARING ON
### COSMETICS HEALTH AND SAFETY ISSUES
### BEFORE THE SMALL BUSINESS SUBCOMMITTEE ON
### REGULATION AND BUSINESS OPPORTUNITIES
### SEPTEMBER 15, 1988

Today the Subcommittee continues its examination of the health and safety issues that are increasingly at stake in the $17 billion U.S. cosmetics industry.

At our July 14 hearing, witnesses told us how dangerous these products can be. The Subcommittee heard how one consumer's hair caught on fire, leaving her permanently disfigured and in constant pain. Cosmetologists explained how they had suffered irreparable nervous system damage, memory loss and severe respiratory problems.

The evidence showed that consumers cannot be sure that the thousands of cosmetic presently on the market are safe. The Food and Drug Administration, the agency responsible for overseeing the safety and efficacy of products, does not have the same broad-reaching authority to regulate cosmetics that it has for foods and drugs.

After the hearing, FDA spokesman Emil Corwin said that cosmetics should be subjected to the same standards as drugs and foods. "We are the first to recognize ... that cosmetic regulations need to be developed," he said.

The industry contends that cosmetic ingredients are generally safe and innocuous. Since the Subcommittee's first hearing on cosmetics, we have assembled information that would indicate otherwise.

We asked the National Institute of Occupational Safety and Health to analyze 2,983 chemicals used in cosmetics. They compared these chemicals with their registry of toxic chemicals. This research indicates that 884 cosmetic ingredients have been reported to the government as toxic substances.

Many of those 884 toxic ingredients produce, or are suspected of producing, harmful side effects. 314 are reported to cause biological mutation, 218 are reported to cause reproductive complications, 778 are capable of causing acute toxicity, 146 are reported to cause tumors and 376 ingredients are reported to cause skin and eye irritations.

More alarming is the fact that of these 884 ingredients, only 56 have been reviewed -- or are being reviewed -- by the industry's Cosmetic Ingredient Review Board to determine their safety and related health effects when used in cosmetic products. The industry's review board may discount these toxic ingredients due to the particular routes of exposure. However, ignoring these reported harmful effects is foolhardy.

In addition, the Subcommittee asked the FDA for a legal analysis of its powers to regulate cosmetics. It appears their powers are extremely limited. The most the FDA could do to protect consumers is seize an occasionally contaminated batch of products or ask manufacturers to change their advertising claims.

The FDA stated in a letter to the Subcommittee dated August 19, 1988 that "(t)he Agency strongly urges cosmetic marketers to conduct toxicological and other tests appropriate to substantiate the safety of their product." But since the FDA cannot require that these tests be conducted, the FDA does not discover the harm a product causes until after a tragic event occurs.

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Even the FDA's limited authority is used rarely. In Fiscal Year 1987, only 1% of the FDA inspections conducted occurred at cosmetic factories, warehouses or other establishments.

Even these limited powers are hard to exercise. False or misleading labeling cannot be substantiated without proof. The burden of proof is on the FDA and, because they cannot ask for the testing data, misleading claims are not easily identifiable.

Secondly, the items listed as prohibited ingredients are almost exclusively unapproved color additives and do not included most toxic substances and even potential carcinogens such as methylene chloride and formaldehyde.

While the industry does have a voluntary, self-regulatory program, it does not review all ingredients nor does it review all formulations. This is clearly no substitute for unbiased government oversight. The industry's voluntary mechanism does even not review every ingredient used in cosmetics.

Although, the Cosmetic Ingredient Review Board (CIR) has only reviewed nearly 300 of the most commonly used cosmetic ingredients, indications are that many years will go by before nearly all of the thousands of ingredients are reviewed. This could mean that as new ingredients are developed, the CIR will fall further and further behind in the only ongoing effort to investigate the safety of the products its members are actively marketing.

Furthermore, the Subcommittee has received criticism from independent sources which indicates that the CIR may not be receptive to all concerned parties before deciding whether a particular ingredient is safe.

In essence, the entire industry's safety mechanism is a piecemeal, patchwork system in dire need of repair.

The government cannot information on specific ingredients and worse, it cannot get information on the possible interactions and formulations of these cosmetic chemicals.

What if the cosmetic ingredients produce a potentially harmful reaction -- either short term or long term? How would we know? Where could we go to find out? As long as the data remains hidden in the pockets of the manufacturers, we will never know the full effects of the ingredients on those who use them.

Today we will hear from the FDA, OSHA, FTC and the industry's trade representatives.

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

STATEMENT

BY

FRANK E. YOUNG, M.D., Ph.D.

COMMISSIONER

FOOD AND DRUG ADMINISTRATION

PUBLIC HEALTH SERVICE

DEPARTMENT OF HEALTH AND HUMAN SERVICES

BEFORE THE

SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

COMMITTEE ON SMALL BUSINESS

HOUSE OF REPRESENTATIVES

SEPTEMBER 15, 1988

FOR RELEASE ONLY UPON DELIVERY

Mr. Chairman:

I am pleased to join you and your Subcommittee today to discuss the Food and Drug Administration's (FDA) regulation of cosmetics. The role of FDA in assuring the safety of cosmetics has been to fulfill the mandate of Congress within the authorities provided to the Agency in 1938 by the Federal Food, Drug, and Cosmetic Act (FD&C) and in 1966 by the Fair Packaging and Labeling Act (FP&L).

## I. INTRODUCTION

This year is the 50th anniversary of the 1938 FD&C Act which, for the first time in history gave FDA authority over cosmetics. In the past fifty years we have seen many changes in the laws covering the products we regulate and in the science that is the basis of our activities as a public health, regulatory agency. The common denominator, both in 1938 and today, is that regulatory decisions, including the extent and scope of the regulation, must be based on sound science. Sound science is an excellent tool to identify public health problems and to prevent or resolve the identified problems.

Congress in 1938 recognized the public health problems associated with cosmetics and addressed them in the laws they enacted based on the science available to them at the time. But science and the cosmetic industry have changed. In 1938, at most only a few hundred ingredients were used to formulate cosmetics, and the industry was small in numbers of manufacturers and marketed products. Today, tens of thousands of cosmetics are in distribution and the number of ingredients used has risen to an estimated 4,000 for producing a multitude of base formulation and an equal number for compounding fragrances.

Regulatory science has also progressed. When the law regulating cosmetics was enacted in 1938, the science was based on a less sophisticated concept for evaluating the safety of chemicals used on the skin: "If you see a reaction, treat it, and then avoid it." Today's science can take into account the effects produced under chronic long term exposure to trace contaminants, in addition to acute toxic effects such as immediate skin irritation, contact allergenicity or systemic reaction resulting from inhalation or ingestion. In 1938, the skin was considered to be an impenetrable barrier to cosmetics or other substances.

As the number of ingredients and products has multiplied through scientific and technological innovation, our ability to measure minute amounts of residue contaminants or other unwanted substances has also taken quantum leaps. At the same time, science has also developed more precise ways to assess risks, taking into account relevant factors such as use and exposure over a lifetime.

Even though much has changed relative to this industry, the question of the need to increase regulatory authority over cosmetics has remained constant: Are there significant public health problems associated with cosmetic use?

During the 1970's, Congress considered amending the cosmetic safety laws and held hearings on the adequacy of the authority Congress gave FDA under the 1938 Act. As a result of those hearings Congress chose not to enact new legislation. In fact, Congress did not enact any new legislation in the past 50 years that increased FDA's authority over the safety of these products.

## II. LEGAL AUTHORITY GRANTED BY CONGRESS

I would like to discuss the statutory framework for regulating cosmetics in some detail to assist your Subcommittee in understanding why we do what we do.

Cosmetics, marketed in the United States, whether manufactured in the United States or imported, must comply with regulations published by FDA under the authority of the FD&C Act and the FP&L Act. A special provision of the FD&C Act, however, exempts coal tar hair dyes as long as manufacturers place a warning of the possible danger on the label and advise the user to make a patch test before applying the product.

The Federal Food, Drug, and Cosmetic Act of 1938, as amended (21 U.S.C. 301 et seq.), defines a "cosmetic" as an article (except soap) intended to be rubbed, poured, sprinkled, sprayed on, introduced into, or otherwise applied to the human body for cleansing, beautifying, promoting attractiveness, or altering the appearance.

Although the term cosmetic has frequently been interpreted as referring to products such as makeup, nail polishes, and perfumes used primarily by women, the term actually applies broadly to products used also by men and women, and on children and infants. For example, baby powders, baby creams, bubble baths, toothpastes, mouthwashes, deodorants, shaving creams, hair tonics and sprays, hair dyes, colognes, and suntan lotions are all cosmetics.

The FD&C Act, through the prohibited acts and adulteration and misbranding sections states that a cosmetic must be:

- free of substances that may make it injurious to users under normal conditions of use (not adulterated);
- packaged in a safe and nondeceptive container (not adulterated and not misbranded);
- produced under sanitary conditions (not adulterated); and,
- labeled with information about the name and location of the product's manufacturer, packer, or distributor and the quantity of its contents (not misbranded).

In order to assure the safety of cosmetic products under the adulteration clause of the FD&C Act, FDA pays special attention to the composition of the products to see that substances that are injurious are not included. Although the Agency does not have the authority to review cosmetic products before they are marketed, FDA maintains surveillance of cosmetics and their ingredients through postmarketing review that I will describe in detail later in my testimony.

FDA issues labeling regulations to assure compliance with the requirements of the two distinct laws, the FD&C Act and the FP&L Act. The identity of the product, the name and location of the manufacturer or distributor, the net contents (weight) statements, and a listing of all ingredients in descending order of predominance are all required by these regulations. Cosmetics which are also drugs must first identify the drug ingredient(s) as "active ingredient(s)" before listing the cosmetic ingredients. In fact, cosmetics bear more informative ingredient labeling for consumers than most other article regulated by FDA: only cosmetic labeling must identify by name all colors used in the product.

The term labeling includes all labels and other written, printed, or graphic matter on or accompanying a product. The label statements required by the FD&C Act must appear on the immediate product container, as well as the outside container or wrapper. The FP&L Act does not require the immediate product containers to bear ingredient labeling. The FP&L Act also does not extend to professional use products that are not sold to consumers.

The FP&L Act requires and authorizes FDA to publish regulations which provide that consumer commodities, including cosmetics:

- o bear label statements of product identity and net quantity (weight) of contents; and
- o bear label statements listing the ingredients, other than trade secrets, in order of descending predominance.

Cosmetics not customarily distributed for retail sale, e.g., hair preparations or make-up products (including skin cleansing or emollient creams) used on consumers by professionals at their place of business, are exempt from the ingredient labeling requirements provided these products are not also sold to consumers for their use at home.

The ingredient labeling regulations authorized by the FP&L Act only apply to the outer "container" or "wrapper" of the cosmetic, so that consumers have the information needed to make an informed decision when they make a retail purchase.

At this point, I want to acknowledge the fact that most ingredients and formulations of cosmetic products are safe for general use under the conditions of formulation. I will now describe how FDA implements strategies to regulate cosmetics under the authority of the two laws just reviewed.

## III. HOW FDA CARRIES OUT ITS MANDATE

We estimate that cosmetic firms in the United States market about 40,000 to 50,000 products that are formulated with about 4,000 ingredients and an equal number of fragrance ingredients. These products are manufactured at 2,000 to 2,500 manufacturing establishments and distributed by 4,000 to 5,000 firms that we have identified. Consumer expenditures for cosmetics in 1987 have been estimated to exceed $18 billion.

To regulate an industry this size, with so much diversity in products and ingredients and in technical complexity, FDA has developed a number of approaches and innovative strategies within the current statutory authorities. These are often interrelated and overlapping and are carried out through:

- Evaluation of consumer complaints of injury and adverse reaction;
- Maintainance of cosmetic registeries;
- Conduct of scientific research on ingredients and development of methods for detection of adulterants;
- Surveillance of the cosmetic industry and its products;
- Consumer and industry education;
- Publication of regulations; and
- Regulatory action against adulterated or misbranded cosmetics.

o Consumer Complaint and Injury Report Evaluation --- We continually encourage consumers and health professionals to report to FDA adverse reactions and the cosmetic products responsible for these reactions. FDA considers these reports an excellent source of information on how products behave under use conditions. In many cases, we can also assist consumers in preventing future adverse experiences. We conduct some degree of investigation on these reports, selectively analyze submitted samples, or carry out certain toxicological or microbiological tests to determine the source of a reaction. Aside from assisting consumers in the safe use of cosmetics, the collected data help us identify products or ingredients that may present a health risk and direct our efforts towards further scientific investigation to eliminate this risk.

As a result of evaluating reports on adverse reactions, FDA has conducted focused studies on specific ingredients which we have then regulated. An excellent example of the importance of consumer complaints in identifying and eliminating a health hazard associated with cosmetics is the discovery of 6-methylcoumarin (6-MC) as a photocontact allergen. Soon after introduction of a new sun exposure product that contained a relatively large concentration of 6-MC in the perfume compound, FDA received several complaints of irritation, swelling, and sunburn-like adverse reactions. Thorough investigations of these complaints resulted in toxicological and clinical studies which identified 6-MC as the causative ingredient. The products in question and other numerous products containing 6-MC were recalled and manufacturers voluntarily discontinued further use of this ingredient in products where use involves exposure to intense sunlight.

o Cosmetic Registries --- Information on the composition of cosmetics and their potential for adverse reactions is also received through the voluntary registration of cosmetic product formulations and experiences. This program was initiated in the early 1970s by a cosmetic industry trade association at FDA's request. The filed formulation data are useful for FDA to determine the typical composition of certain types of cosmetics and the specific composition of those registered. The filing of product experiences permits us to determine adverse reaction norms for the various product categories. We do then compare the adverse reaction reports and identify products that may need further investigation.

I have attached to this testimony a summary of the pertinent data on the cosmetic industry participation in these programs as of July 1988. As can be seen from the attached tabulation, it is unfortunate that this program does not enjoy greater industry participation, in spite of the efforts made by the Cosmetic Toiletry and Fragrance Association to increase registration.

- Surveillance of the Cosmetic Industry and its Products --- The FD&C Act authorizes the Agency to inspect cosmetic manufacturing establishments, including pertinent equipment, finished products, raw materials used as ingredients, containers and labeling, and to collect samples for examination and investigation. During FY 1987 a typical year, the FDA inspected 213 cosmetic manufacturers out of a total of 20,298 inspections of all industries regulated by the Agency, and collected numerous samples for further examination of labeling and microbiological or toxicological testing as appropriate.

- Enforcement and Regulatory Actions --- The authority given to FDA in 1938 to prohibit the sale in interstate commerce of cosmetics that are adulterated or misbranded was, and still is, primarily enforced after distribution on a product-by-product basis. The 1938 Act places the burden of proof that a cosmetic product, like a food product, is either adulterated or misbranded, or both on FDA.

When a cosmetic has been determined to be adulterated or misbranded, we act according to the degree of the public health risk. If the hazard warrants an immediate action, the Agency urges the responsible firm to initiate a product recall. When firms do not agree, the Agency has the authority under the FD&C Act to proceed in a Federal court against the violative product and request seizure. FDA will also make public announcements about the risk posed by some products. The Agency may also request the court to enjoin the manufacturer from further distributing that product. Additionally, rulemaking has been another FDA strategy to prevent the further use and consumer exposure to hazardous ingredients and products. Regulations prohibit the use of the neurotoxic hexachlorophene and mercury compounds, of photocontact allergenic halogenated salicylanilides, and of the ozone-damaging chlorofluorocarbon propellants of aerosol products.

Shampoos, cream rinses, and eye area cosmetics, i.e., mascaras or eye shadows, contaminated with pathogenic microorganisms which may cause blindness, have always been removed from the marketplace through recall or seizure action. Recalls and seizure actions were effective against methyl methacrylate-containing nail builders and against various imported eyelash dyes containing hazardous dye ingredients.

At other times, the industry has voluntarily discontinued use of the hazardous product. Examples of hazardous cosmetic ingredients voluntarily discontinued are the fragrance ingredients acetylethyl tetramethyl tetralin (AETT) (a neurotoxin), 6-methylcoumarin (a photocontact sensitizer), and musk ambrette (which may be both neurotoxic and sensitizing).

o Consumer and Industry Education --- A substantial amount of time and effort is invested at all levels of the Agency in educating consumers about the safe use of cosmetic products, including their inadvertent or intentional misuse and consequences. FDA provides consumers, manufacturers, trade and professional associations, and the press with information on health hazard issues, regulatory requirements and actions, and other pertinent issues related to cosmetics. We have found that, as in other product areas, consumer education and high quality products are vital links to optimal product use and consumer safety. It is important to have truthfully and informatively labeled packages with adequate directions for use. At first glance, the label of a product would not seem to have too much to do with its safety, but

FDA has found that the truthful labeling with adequate direction for use in fact contributes to the safe use of the product.

As an example of consumer education, FDA CONSUMER, an award winning publication, has published many article which focus on the safe use of cosmetics. The publication presents critical issues from a consumer's perspective.

- Publication of Labeling Regulations --- In addition to taking enforcement actions and issuing public announcements, FDA also issues labeling regulations under the authority of the FD&C Act to provide warnings to consumers because of demonstrated safety problems with certain products. Cosmetics which may be hazardous to consumers when misused must bear appropriate label warnings and adequate directions for safe use. These warnings must be prominent and conspicuous. For example, because many consumers and pediatricians reported urogenital infections from repeated use of bubble bath products, FDA adopted a regulation requiring that children's bubble bath products bear a warning statement. Also, self-pressurized containers and feminine deodorant sprays likewise must bear warning statements. These warnings must appear on professional as well as consumer products.

And finally, in addition to labeling regulations for safety hazards, the FD&C Act also requires us to protect the consumer from deceptively labeled products. Public awareness about fraudulent label claims is increasing. Cosmetic labels must bear cosmetic claims, not drug claims. If a label claims to prevent or to treat disease or otherwise affect the structure or function of the human body, it may be considered a drug for regulatory purposes. If FDA considers it to be a new drug, the marketer carries the burden of proving it is safe and effective before it can be legally marketed. It is interesting to note that in August 1939, FDA published a "Trade Correspondence" (TC) a document used to inform the industry of the Agency's regulatory positions which listed typical examples of product names and claims that were regarded as false or misleading for cosmetics under Section 602(2) of the 1938 Act. Examples of these claims include phrases such as "rejuvenating creams," "hair restorers," "deep pore cleaners," "eyelash grower," "nourishing cream," "wrinkle eradicator," stimulating cream," and the list goes on. The Agency stated at that time that a survey taken of the products on the market "indicates the probability that a substantial proportion of the cosmetic industry has not realized that certain names and statements . . . may contravene requirements of the statute which have now become effective." It appears that 50 years later, some of these same claims are again being used.

IV. INTERNATIONAL ACTIVITIES --- FDA strategies also include our involvement in international activites to further marketing of safe cosmetics. FDA regularly provides information to other governments, international organizations, and foreign exporters concerning U.S. legal requirements, and our regulatory programs and actions, including the reasons for these actions. We share our expertise with other governments and, in some circumstances, provide technical assistance when requested by our counterparts in other nations. Through our foreign visitors program, FDA has scheduled meetings with over 500 visitors from 50 different countries and organizations. FDA officials participate in many international cosmetic meetings.

## V. COOPERATION WITH INDUSTRY TO SOLVE PROBLEMS

As I have stated often as Commissioner, the production of safe, truthfully labeled, and otherwise high quality products largely depends on the degree of cooperation between the regulator and the regulated. This tenet applies particularly to the less-regulated cosmetic industry. Furthermore, this framework for cooperation is in keeping with legislative intent of the 1938 Act, which places the primary responsibility for assuring safety of cosmetics on the industry rather than on FDA. Based on my association with the cosmetic industry, I believe that they are as interested in the safety and credibility of their products as we are at FDA. This industry must maintain the confidence of the consumers who purchase the cosmetics, because their products differ from food and drugs in that cosmetic products are not necessary to sustain life, but contribute to the aesthetic quality of life.

Cooperation between industry and FDA has to a great extent been achieved through industry's trade associations which have maintained effective working relationships with FDA through the years.

There are many good examples of cooperative and individual efforts by the cosmetic industry, as represented by its trade associations, over the years. As stated before, in the early 1970s, the Cosmetic, Toiletry and Fragrance Association (CTFA) petitioned the FDA to publish guidelines for voluntary registration of manufacturing establishments, proprietary raw materials, formulations, and consumer-reported product experiences. Even before that, in 1966, the fragrance manufacturers, through their trade association established the Research Institute for Fragrance Materials (RIFM) to carry out research on the safety of fragrance raw materials. In 1976, the CTFA announced the creation of the Cosmetic Ingredient Review (CIR) program to review the scientific literature for information on raw materials used as cosmetic ingredients. The CIR is an independent panel of internationally recognized scientific experts that reviews these data.

Additionally, CTFA, in emphasizing their self-regulatory program, has published numerous useful guidelines on how to test cosmetic products for safety, preservation, and product integrity.

Product preservation also has been a concern of my Agency. FDA has dedicated resources for studies to determine the adequacy of cosmetic preservation systems. This is important when you consider that whenever a human hand touches a cream or uses a multi-use applicator for a cosmetic, microorganisms, including pathogens, have been introduced into that packaged product. FDA is conducting studies to develop predictive methods for the determination of the adequacy of these preservation systems which are critical in preventing the proliferation of the pathogens.

The Independent Cosmetic Manufacturers and Distributors (ICMAD), a trade association representing mostly small cosmetic manufacturers and marketers, has held joint workshops with FDA on topics of labeling, good manufacturing practices, and other regulatory interests.

All these cooperative efforts are commendable and we will continue similar cooperative efforts when appropriate. There are many areas where cooperation between the regulated industry and the government regulator could be further improved.

## CONCLUSION

In summary Mr. Chairman, I want to emphasize that the dominant concern of the FDA, as a public health agency, is the safety of the products we regulate for the consumers who use them. There are cosmetic products with labeling which bear claims that the products are intended to change the cellular structure of the skin, thus claiming it would be wrinkle free and younger looking. With safety considerations at the forefront of our concerns, we have taken action against these products which, because of their claim to have physiological effects on the body, cross over the line into the area of drugs. If in fact these physiological changes do occur from use of these products, we must have assurances that these changes occur in a sage manner. Manufacturers must demonstrate to FDA that their products are safe and effective for their intended use. If any of these firms have data to demonstrate the safe and effective use of their products, these data must be submitted to FDA for approval before marketing their product. As a result of our actions, some of the firms marketing these products have relabeled and removed these drug claims.

There are also legally marketed drugs which are used for purposes that would be considered cosmetic by many. These drugs, such as Minoxidil, which was recently approved by FDA to treat baldness, went through the new drug approval process where the manufacturer demonstrated to FDA the drug's safety and effectiveness. Retin A is currently under investigation by the sponsor. Other examples of drugs also considered as cosmetics are over-the-counter products such as fluoride toothpaste, anti-perspirants, and sun screens. These products are marketed in accordance with monographs which specify safe and effective ingredients for these products.

As a physician, another issue of concern is the availability of information regarding hazardous ingredients in cosmetics uses by cosmetologists in their workplaces. The professionals who use these products on a daily basis over a long term, as well as the person on whom the product is used should be able to ascertain what chemicals are in these products. The professional and the consumer exposed to these products, as well as the physician who may be involved in any potential treatment for disorders related to the use of any of these toxic chemicals, need sufficient information for safeguarding health. I have recently been informed that the Occupational Safety and Health Administration (OSHA) has in place a comprehensive regulation on chemical hazards that requires manufacturers of cosmetics to evaluate the hazards of these products and transmit complete hazard information to purchasers of these products. In addition, the OSHA regulation requires employers of cosmetologists to inform their employees about these chemical hazards and to train their employees to avoid danger exposures. FDA supports the development and implementation of the OSHA standard, and will continue to work with OSHA and other Federal agencies in assuring that cosmetologists and their clients are protected from hazardous chemical exposures in the workplace. Consumer protection in the area of cosmetics, from hazardous or misbranded products, depends largely on effective communication, namely, informing consumers and industry about our safety and labeling concerns working closely with cosmetic manufacturers on these matters before they even become regulatory issues.

Consumer protection in the area of cosmetics, from hazardous or misbranded products, depends largely on effective communication, namely, informing consumers and industry about safety and labeling concerns and working closely with cosmetic manufacturers on these matters before they ever become regulatory issues.

To conclude Mr. Chairman, let me state that it is in keeping with the intent of Congress that FDA programs place the responsibility for the safety of cosmetics on the industry. Our role is to monitor the safety of these products, and as I have noted, other agencies play important roles in this. This is good regulatory approach. There is substantial authority already existing in law to support this approach. While regulations can contribute to making these products safer, even the most stringent regulatory requirements cannot guarantee absolute safety and quality assurance. However, safety and quality assurance can be improved with active cooperation among those who make the products, those who use them, and those who regulate them. Our current law and regulations are designed to meet these goals.

Mr. Chairman, that concludes my formal statement. I will be glad to respond to any questions you or members of your Subcommittee may have.

# SUBMISSION FOR THE RECORD

Page: 13

Line: 289

COMMITTEE ON SMALL BUSINESS

SUBCOMMITTEE ON REGULATIONS AND BUSINESS OPPORTUNITIES

HOUSE OF REPRESENTATIVES

SEPTEMBER 15, 1988

REQUEST: None --- Dr. Young offered for the record copies of FDA Consumer articles on cosmetics.

SUBMISSION: Reprints of "Cosmetic Allergies", "Questions Of Substance(s) Concern Cosmetic Users", and "Erasing Wrinkles: Easier Said Than Done."

# Cosmetic Allergies

*by Dori Stehlin*

Whether or not a permanent improves a person's appearance is a matter of opinion. But when Carolyn, a secretary in Rockville, Md., arrived at her wedding shower one May evening, it was easy to see that the permanent she got at a beauty salon the day before had not produced the desired results. While the chemical treatment did give her curly hair, it also gave her a red, swollen face.

"I tried to cover it up with makeup," she said, "but it didn't help much. I was so embarrassed at the shower. Thank goodness I didn't wait until right before the wedding."

Carolyn had a case of cosmetic contact dermatitis—an acute allergic inflammation of the skin caused by contact with various substances found in cosmetics. In addition to the redness and swelling, her skin was weeping and covered with papules (small, solid elevations of the skin)—all classic symptoms of contact dermatitis.

Cases of contact dermatitis from cosmetics are rarely painful or life-threatening, but they sometimes can be so uncomfortable the unhappy victim will seek a doctor's care. The frequency of adverse reactions to cosmetics that require a physician's care is approximately 210 per 1 million cosmetic products purchased, according to information from a Food and Drug Administration survey and a study of cosmetic reactions conducted by the North American Contact Dermatitis Group, a task force of the American Academy of Dermatology.

Skin-care products, such as facial cleansers and moisturizers, were associated with the largest number of cosmetic allergic reactions in the study, which ran from September 1977 to August 1983. Hair preparations in general, including hair dyes, formed the second largest group, and facial makeup, such as foundation and blusher, was third. Other problem products included nail preparations and fragrance products.

As for the types of ingredients that cause the allergic reactions, the study found that fragrances and fragrance ingredients were responsible for the greatest number. Preservatives were next, followed by p-phenylenediamine (found in hair dyes), lanolin, the hair-waving ingredient glyceryl monothioglycolate, and propylene glycol (a skin softener).

What caused Carolyn's reaction? It may have been a chemical in the permanent itself or one of the many ingredients in the other products she used before and after the permanent—the shampoo, conditioner, neutralizer. She never did find out, and she's still worried that the ingredient will be in some other products she may use.

"It is important to find out which ingredient causes an allergic reaction, so a consumer can look for that ingredient in other products," said Heinz Eiermann, director of FDA's Division of Colors and Cosmetics. Yet half of the patients and their dermatologists in the contact dermatitis group study did not at first realize that a cosmetic was responsible for the dermatitis. Dr. Robert M. Adams, clinical professor of dermatology at Stanford University and a member of the contact dermatitis group, called that an important—and surprising—finding.

Why don't the patients or doctors suspect a cosmetic? One possible reason is that a product can be used without a reaction for years before "suddenly" causing an allergic problem. Repeated exposure to the offending ingredient can build up sensitivity.

"A lot of people can walk through poison ivy without any kind of reaction, but after a while their cells start to recognize this antigen and they start to react to it," said John Sanders, a dermatologist with FDA's Center for Drugs and Biologics. "The same thing can happen with cosmetics. Patients will tell me 'I've been using this product for several years; it can't be.' But there's always a first time."

What should be done if a reaction occurs? First, stop using *all* cosmetics. To help relieve the itching, 0.5 percent hydrocortisone cream can be applied, several times a day if needed. Other treatments include wet compresses and Aveeno (an oatmeal preparation). (See "The Itch of the Great Outdoors" in the June 1986 *FDA Consumer.*)

A mild reaction should clear up in seven to 10 days. For severe reactions or ones that last longer than 10 days, a doctor may prescribe a stronger topical steroid preparation or oral medication.

Once the reaction is completely over, cosmetics can be tested, one by one, to find the guilty party. "Before putting a product all over the face and breaking out, place a little on the forearm and watch it for at least 24 hours," FDA's Eiermann advises.

Since consumers use an average of 12 cosmetic products, more or less, at the same time, it may take a while before the offending product is found. But there are a few things to watch for to make the detective work easier. Was a new product used only a few times before the reaction occurred? It should be tested first. Although sensitivity to an ingredient has to build up before a reaction occurs, just two applications of that ingredient may be enough. Even a new bottle or jar of a product used before can be the cause of the problem. Manufacturers are constantly reformulating cosmetics—a new ingredient may have just been added.

HAIR SPRAY
UNSCENTED
acrylamide Acrylates Buty
Methacrylate Copolymer
cone, Aminom
cone Copolyol, Fragrance.

***Avoiding fragrances, the leading cause of allergic reactions to cosmetics, requires careful label reading. Many products are like the hair spray whose label (above) says unscented on the front of the can, but lists "fragrance" as an ingredient on the back.***

Cross-sensitization can also cause problems, particularly with new cosmetics. Cross-sensitization involves closely related chemicals, where a person sensitive to ingredient A may have an allergic reaction when chemically related ingredient B is applied.

After finding out which product was involved in the allergic reaction, the next step is finding out which ingredient actually caused it. FDA requires cosmetic ingredients to be listed in descending order of predominance; that is, the ingredient that makes up the largest part of the product is listed first. Color additives and ingredients that make up no more than 1 percent of the product are exceptions. They can be grouped together in any order. If the problem product lists an ingredient on the label that isn't in any other cosmetics you've used without incident, then that is probably the culprit and should be avoided, no matter what product it is in.

But what if a unique ingredient can't be found on the label of the reaction-causing product? It may be hidden behind the word "fragrance." Only the word fragrance—not the name of the actual scent-giving ingredient—is required on cosmetic labels. In any case, this is when a dermatologist can do a series of ingredient patch tests.

In a patch test, a small amount of the suspect ingredient is applied to the skin and covered with a bandage. Tests are usually done on the back since there is enough room there to do a lot of tests at once. The patches are left in place for 24 to 48 hours to see if redness, rash or any other sign of allergic reaction occurs.

Because fragrance ingredients are the most likely cause of an allergic reaction, testing with those ingredients would be the most likely place for the dermatologist to start. But the process of fragrance testing is complicated. A perfume may consist of 10 to 300 separate components, and the formulas are secrets manufacturers don't want to (or have to) divulge. But manufacturers may, upon request, send a dermatologist different fragrance mixtures identified only by a letter. The dermatologist can then patch test each mixture, and get the separate components of any mixture that gives a positive result from the manufacturer and patch test with those. If a component gives a positive result, the physician can find out if that specific fragrance ingredient is in a specific product. But the manufacturers won't divulge every product that contains that fragrance.

Because of the secrecy, to play it safe

### *Types of Cosmetics that Cause Allergic Reactions*

This table shows the types of cosmetics that were found to have caused allergic reactions in a study of 713 patients between 1977 and 1983. The study was funded by FDA and performed by 12 dermatologists who were members of the North American Contact Dermatitis Group, a task force of the American Academy of Dermatology.

| Product Category | Percent of Cases |
|---|---|
| Skin-care products (lotions, creams, etc.) | 28 |
| Hair preparations (including colors) | 24 |
| Facial makeup | 11 |
| Nail preparations (polish, remover, etc.) | 8 |
| Fragrance products (perfumes, colognes) | 7 |
| Personal cleanliness products | 6 |
| Shaving preparations | 4 |
| Eye makeup | 4 |
| Suntan and sunscreen products | 3 |
| Oral hygiene products | * |
| Bath preparations | * |
| Baby products | * |
| Products not specified | 4 |

** Less than 1 percent*

### *Cosmetic Ingredients that Cause Allergic Reactions*

This table shows the cosmetic ingredients that most often caused allergic reactions in the North American Contact Dermatitis Group study.

| Ingredient | Percent of Cases |
|---|---|
| Fragrance ingredients | 30 |
| Preservatives (antibacterial) | 28 |
| *p*-Phenylenediamine | 8 |
| Lanolin and derivatives | 5 |
| Glyceryl monothioglycolate | 5 |
| Propylene glycol | 5 |
| Toluenesulfonamide/formaldehyde resin | 4 |
| Sunscreens and other ultraviolet absorbers | 3 |
| Acrylate or methacrylate | 2 |
| Others | 10 |

those allergic to fragrances should only use products that are labeled "fragrance-free" or "unscented." But even these products sometimes contain small amounts of fragrances to mask the fatty odor of soap or other unpleasant odors in "unscented" antiperspirants and vaginal lubricants. They are also used in cosmetics labeled "lightly scented" and those with "nonlingering" fragrance. Although these fragrances make up less than 1 percent of the cosmetics they're in, they could cause problems.

If "fragrance-free" doesn't always mean that there isn't any fragrance in the product, what about the other claims aimed at people concerned about allergic reactions? Do "hypoallergenic" and "allergy tested" and other such label claims mean there's no chance of a reaction? Unfortunately, no. There's always a possibility that someone somewhere will have an allergic reaction.

The prefix "hypo" in this case means "less than." "Hypoallergenic" on the label means the product is *less* likely to cause an allergic reaction. But there are no standards on how a manufacturer decides when a product is hypoallergenic. Although some manufacturers do clinical testing, others may simply omit perfumes or other common problem-causing ingredients.

"Dermatologist-tested" is another common label claim on cosmetics. It only means that a skin doctor has tested the product to see if it will generally cause allergenic problems. Other label claims that, unfortunately, carry no guarantee that they won't cause reactions include "sensitivity tested," "allergy tested," and "nonirritating."

Replacing known allergens with chemicals that not only have a lower sensitizing potential but also are safe in other ways and don't alter the properties of the product is extremely difficult. The fragrance industry is trying to eliminate ingredients that cause adverse reactions. The International Fragrance Association has a list of chemicals they recommend not be used at all or at only limited concentrations. And the Cosmetic Ingredient Review Panel, a group of experts convened by the cosmetics industry, is reviewing the toxicology of the more than 4,000 ingredients used in cosmetics.

Yet, except for eliminating fragrances and known allergens such as lanolin, the basic ingredients in products both with and without hypoallergenic claims are the

### *Parts of the Body Affected by Cosmetic Allergies*

This table shows the parts of the body that were affected by allergic reactions to cosmetics in the North American Contact Dermatitis Group study.

| **Body Site** | **Percent of Cases** |
|---|---|
| Face | 37 |
| Eyes | 12 |
| Forearms | 12 |
| Armpits | 6 |
| Ears | 4 |
| Entire body | 4 |
| Neck | 3 |
| Scalp | 2 |
| Mouth | 2 |
| Upper arms | 2 |
| Fingers | 2 |
| Fingernails or toenails | 1 |
| Other | 6 |
| Unknown | 7 |

same. Although the differences between products with hypoallergenic claims and those without are small, sales of hypoallergenic cosmetics are no longer limited to people with serious skin problems, according to *Advertising Age* magazine. John Bard, president of Physicians Formula cosmetics (a line of hypoallergenic products), said that more than 50 percent of Americans think they have "sensitive" skin.

But how many people actually have allergic reactions to cosmetics? In the American Academy of Dermatology study, cosmetic ingredients were the cause of the contact dermatitis in only 713 out of 13,216 patients—just over 5 percent. But the actual incidence of reactions is hard to assess. Instead of going to a dermatologist and trying to pinpoint the ingredient that caused the reaction, many consumers just stop using the product they suspect is at fault. On the other hand, not every rash is an allergic reaction.

Everyone's skin is sensitive, in some degree, to the harsh materials in products such as depilatories (hair removers) and hair straighteners. The rashes these materials cause are usually not true allergic reactions—the skin is simply irritated.

For some people, the harsh ingredients that cause irritation must be completely avoided. However, others may still be able to use those products if they use less and don't leave it on as long.

Consumers and their dermatologists should report cosmetic adverse reactions to FDA's Division of Colors and Cosmetics, 200 C St., S.W., Washington, D.C. 20204. "Although we may not be able to help the individual consumer," FDA's Eiermann said, "this information will tell us that there may be a problem with that product. If we do see a cluster of adverse reactions associated with a specific product, we can then investigate further and remove the product from the market, if warranted, to protect everyone."

The cosmetic manufacturers also want to hear about any allergic reactions to their products, according to Page Blankingship, manager of communications for the Cosmetic, Toiletry and Fragrance Association. "Most of the people in the cosmetic industry are pretty wise," FDA's Sanders said. "They've been around and they're not going to put a product out there that is going to cause reactions if they can help it."

Even with the cosmetic industry's efforts to eliminate problem ingredients, consumers who feel they may be prone to allergic reactions should still use some caution to avoid them. Here are some tips:

- A do-it-yourself patch test may be done with any new product. Put a small amount of the product on the inside of the elbow and cover it with a bandage. Do this on the same spot twice a day for four days. If a rash appears, don't use that product. Even if the patch test is negative, continue to watch for a reaction for a few days after starting normal use of the cosmetic.
- Don't try more than one new product at a time. Wash your hands, and use clean applicators when applying cosmetics to prevent contamination with bacteria. And never apply cosmetics to skin that is already irritated or inflamed.
- A patch test should be done a few days before any professional hair treatment, such as a permanent or hair coloring. It's worth the extra effort of making two trips to avoid an experience like Carolyn's. Although the ingredient labeling required on retail cosmetics isn't required on products sold to beauty parlors, that information may be available from the manufacturers. Tell your beautician of any ingredient you know you're allergic to.
- Read the label of any new cosmetic before you try it, and avoid any that contain an ingredient that caused a reaction in the past.

While even diligent label reading and patch testing can't guarantee reactions won't occur, don't give up hope. Carolyn didn't. A few months after her disastrous permanent, she decided to gamble on another. She went to a different beauty salon and made sure the beautician used a different brand of permanent. And she got a patch test. The test was negative, so she went ahead with the permanent. And this time she only got what she paid for—curly hair. ■

*Dori Stehlin is a member of FDA's public affairs staff.*

# Questions Of Substance(s) Concern Cosmetic Users

*Rousseau once said, "Man can be cured of every folly but vanity." From the amount of money spent on cosmetics these days, it's safe to say that times haven't changed much. Last year more than $10 billion was spent on hair preparations, mouthwash, makeup, shaving cream and perfume. But along with our love for looking pretty is a need to reassure ourselves about the safety of cosmetic products. To help people who are concerned about what's in the cosmetics they use, here are some answers to typical questions received in the mail by the Food and Drug Administration. The answers were prepared by experts in FDA's cosmetics division.*

Q. *I want to inquire about a substance called BHT found in some soap products. Is it a carcinogen?*

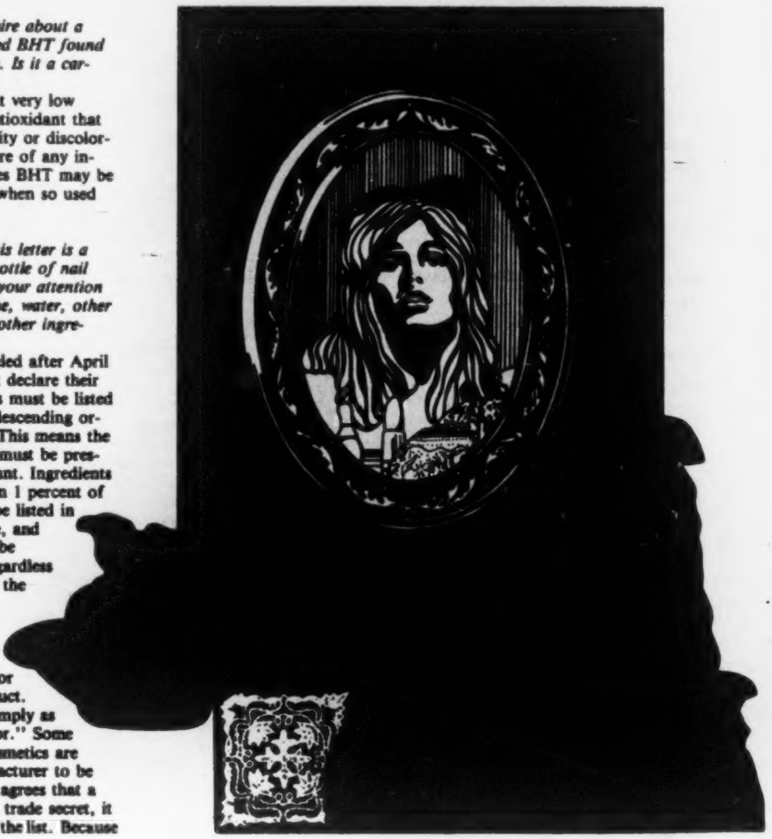
A. BHT is used at very low levels as an antioxidant that protects against rancidity or discoloration. We are not aware of any information that indicates BHT may be harmful or cancerous when so used in soap.

Q. *Attached to this letter is a label from a bottle of nail polish remover. I call your attention to the contents: acetone, water, other ingredients. What are other ingredients?*

A. Cosmetics labeled after April 15, 1977, must declare their ingredients. Ingredients must be listed by uniform names in descending order of predominance. This means the first ingredient shown must be present in the largest amount. Ingredients that constitute less than 1 percent of the product need not be listed in order of predominance, and color ingredients may be listed in any order, regardless of the amount used in the product.

The ingredient list is not required to include the names of specific fragrances or flavors used in a product. These may be listed simply as "fragrance" or "flavor." Some ingredients used in cosmetics are claimed by the manufacturer to be trade secrets. If FDA agrees that a specific ingredient is a trade secret, it need not be carried on the list. Because of this and the complexity of most fragrance formulas, these substances may be listed as "fragrance" on the label.

Thus, the designation "and other ingredients" on the label of this polish remover is an FDA-approved way to describe ingredients that are recognized as trade secrets and which



the manufacturer is not required to reveal.

Q. *Does using cosmetics such as eye liner, eye shadow, blush, a foundation, or any other cosmetic for that matter, have any long-term effects?*

A. Very little is known about the long-term effects of cosmetics. A long-term effect may be systemic and not just an irritation on the surface of the skin. Many ingredients can penetrate the skin. Skin penetration studies are now under way to determine likely chronic effects of some cosmetic ingredients from long-term use.

Q. *A highly advertised body spray product contains the following ingredients: SD alcohol 40B, isobutane, propane, fragrance, propylene glycol. While the advertising of this product entices consumers to buy it because of its seemingly sensuous smell, it contrasts with the warning on the label that states: "Intentional misuse by deliberately concentrating and inhaling contents can be harmful or fatal." Which of the listed ingredients would cause harmful or fatal consequences if inhaled directly and why would the manufacturer put a dangerous chemical in the product?*

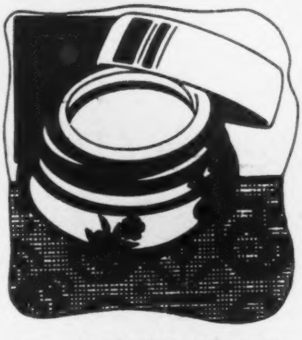
A. The problem is not one of toxicity of any particular ingredient under usual use conditions but of misuse causing oxygen deprivation. Such a warning is required for self-pressurized containers in which the agent used to expel the product is partially or wholly a halocarbon or hydrocarbon. Such propellants have been responsible for the deaths of persons, usually juveniles and adolescents, who concentrated the vapors from such products and inhaled them to induce a euphoric effect, or "high."

According to reports of these cases, the sprays have been concentrated in a number of ways, often by spraying the contents of the container into a plastic bag.

The required warning statement is intended to caution against deliberate rather than accidental misuse. FDA does not have any information that injuries or deaths have ever resulted from normal use of the products involved.

Q. *Are too many permanent waves bad for the health? Do they have any relationship to cancer?*

A. Generally speaking, permanent wave products present no hazard to the consumer when used according to directions on normal healthy hair and scalp, although some consumers may occasionally experience minor itching and scalp reddening or, in some cases, an allergic reaction.



Q. *An advertisement for a cosmetic cream claims that it "has been FDA-cleared as a multifaceted moisturizing, oxygen-transporting cosmetic preparation." Is this true?*

A. The advertisement mentions that this product has been "cleared" by FDA. This statement is untrue. Firms that manufacture cosmetics are neither required to register their company nor to obtain premarket FDA approval for their formulas.

Some statements made for products are in the nature of "puffery" to promote the product. Cosmetic manufacturers often claim their products contain some secret ingredient that is superior to the ingredients used by other brands or some magic formula that will accomplish extraordinary results. But the great majority of cosmetic products in any category—lipstick, face creams, etc.—basically are similar in composition. A popularly priced cream or lotion usually is just as effective in keeping the skin soft as the most expensive face cream. In the expensive cream the buyer may be paying for a pretty jar, an appealing fragrance, or a feeling and aura of exclusivity.

Q. *I am interested in obtaining the name of a hair coloring that would be nonallergenic and would not contain any* coal-tar hair dye.

A. As a regulatory agency, the Food and Drug Administration is not permitted to recommend brand-name products. Even if permitted, it would be unwise to do so, since *any* ingredient in any product may cause a reaction in some sensitive person.

Coal-tar hair dyes are exempted from the adulteration and color additive provisions of the Food, Drug, and Cosmetic Act if the labels bear a caution statement alerting consumers to the risk of skin irritation.

The warning label is as follows:

"Caution—this product contains certain ingredients which may cause skin irritation on certain individuals and a preliminary test according to accompanying directions should first be made. This product must not be used for dyeing the eyelashes or eyebrows; to do so may cause blindness."

If a label bears this warning statement, the additional measures that FDA can take to protect the public are severely limited unless Congress repeals the exemption for coal-tar products. In the past, many bills have been proposed by Congress, but none has passed.

# ERASING WRINKLES:

1
Wrinkle Free

# Easier Said Than Done

*by Dori Stehlin*

> *"When your friends begin to flatter you on how young you look, it's a sure sign you're getting old."*
>
> —Mark Twain

Few events are more dreaded—and less serious—than the appearance of that first wrinkle. But, unlike that other infamous sign of aging, the first gray hair, which can be quickly and surreptitiously plucked out, that wrinkle is here to stay.

Or is it? A creamy flood of new cosmetic products seems to promise not only to prevent new wrinkles, but also to erase the old ones. The price tags for these modern fountains of youth are usually high, but many think no price is too dear for an unlined face.

But the truth is, it's never been scientifically proven that any of these cosmetics actually gets rid of wrinkles. So what about all those advertising claims that promise to send those wrinkles packing?

If a company claims that its product can affect the skin below the surface—for example, can repair cells or make the skin "function as if it were young again"—FDA may consider the product a drug for regulatory purposes. If FDA considers it to be a new drug, the manufacturer must prove that it is safe and effective before it can be legally marketed. None of the currently marketed wrinkle-fixers has a new drug approval.

FDA has already determined that several companies are making drug claims on some of their skin treatment products. In Regulatory Letters sent beginning April 17, the agency told those companies that the claims "represent and suggest that the articles are intended to affect the structure and function of the human body, and that the products are adequate and effective. Because of such claims the products are regarded as drugs.

"Also, we are unaware of any substantial scientific evidence that demonstrates the safety and effectiveness of these articles for their intended uses, nor are we aware that these drugs are generally recognized as safe and effective for their intended uses. Therefore, the products are new drugs. . . ."

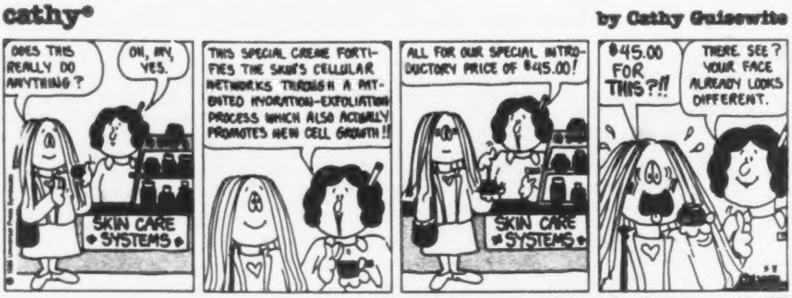
In order to keep making claims that these products alter the skin's functions, the companies must file applications for new drug approval that include data from clinical studies that prove safety and effectiveness. If they don't file applications for new drug approval or stop making the drug claims, FDA is prepared to "take appropriate regulatory sanctions such as seizure or injunction," according to the letters.

As long as the effectiveness of these products is in question, the answer for those who want an unlined face is to not get wrinkles in the first place. Unfortunately, that's impossible. While some wrinkles can be prevented by staying out of the sun, aging skin won't stay unlined forever.

What happens to adult skin to make those wrinkles appear?

In young, undamaged skin, the dermis—the dense layer of tissue beneath the thin, outer epidermis—contains flexible, soft, resilient connective tissue called elastic fibers. But as the skin ages, or is damaged by the sun's ultraviolet

*The truth is, it's never been scientifically proven that any of these cosmetics actually gets rid of wrinkles.*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THERE. SEE? YOUR FACE ALREADY LOOKS DIFFERENT.

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rays, the structure of these fibers deteriorates.

The deterioration begins with excessive production of abnormal fibers. This is an inevitable part of aging even without sun exposure. "To get a wrinkle you have to have too much skin," says Dr. Albert Kligman of the University of Pennsylvania's Department of Dermatology. "It's got to sag. That's mainly the result of an excessive amount of tissue."

The elastic fibers eventually break down into a fiberless mass. Once that happens, mechanical stress will cause wrinkles to appear. "You have to use your facial muscles very energetically to work those lines into that sagging tissue," Kligman explains. Unlike young, normal fibers, sagging tissue, when stretched, can't snap back. The tissue remains stretched—and wrinkled. Kligman compares wrinkles of the skin to grooves in an old well-used glove.

The facial muscles used to inhale a cigarette may cause some wrinkles, according to a study published in the December 1985 *British Medical Journal*. The study said "smoker's face" is characterized by wrinkles that spread out at right angles from the upper or lower lips or corners of the eyes.

Even in skin that has been kept in the dark, the elastic fibers will eventually deteriorate. However, the majority of this deterioration isn't visible until after the age of 70. On the other hand, wrinkles from sun damage can start to appear as early as 30.

The only way to prevent this premature damage is to stay out of the sun or use a strong sunscreen. In fact, a cosmetic's claim that it "prevents new wrinkles" usually means it contains a sunscreen.

In addition to sunscreens, many products contain moisturizers for dry skin. Dry skin doesn't cause wrinkles. But moist, soft skin—even if it is wrinkled—certainly looks better than rough, scaly, dry skin.

Moisturizers form a seal that keeps water from evaporating from the skin's surface cells. More water in the cells means greater flexibility, softness and smoothness. This effect can come with equal success from a $65 bottle of exotically named cream or a plain jar of petroleum jelly.

The important point here is that any moisturizer's results are only temporary. But how temporary differs from product to product.

A 10-year dermatological study led by University of Pennsylvania researchers tested different moisturizers on young women (mainly college students) who had very dry skin on their legs. The study found that using petrolatum (petroleum jelly) for 14 days almost eliminated the roughness, cracks and scales—typical signs of common dry skin. The beneficial effects could be seen for about two weeks after the last application. On the other hand, the moderate dry-skin relief from cold cream only lasted three to four days after use was stopped.

The runner-up to petroleum jelly was lanolin. Mineral oil, vegetable oils and lard are at the bottom of the list in terms of major, lasting relief from dry skin. Mineral oil's relief lasted only one day.

The study, presented at the Safety and Efficacy of Topical Drugs and Cosmetics Symposium in 1982 in Philadelphia, was not able to substantiate claims that humectants (moistening agents) attract moisture or improve a moisturizer's

## Wash and Wear

How often should people wash their faces?

"As little as they can," says University of Pennsylvania dermatologist Albert Kligman.

There aren't any definite rules on how often to wash, says FDA dermatologist John Sanders. He explained that, first, each person's needs are different. For example, he said, an office worker doesn't get as dirty as a car mechanic. And second, an individual's washing schedule can be affected by what he or she did on a certain day or the time of year.

But he agrees with Kligman that less is better. "The public has been brainwashed into thinking that they have to be cleaner than clean," he said. "Although the majority of the public can get away with too much washing because their skin is pretty tolerant, people should realize that soaps are irritants."

In addition to irritation, almost all soaps dry the skin because they remove skin lipids (fats) and the skin's own moisturizing substances. "Moist skin contains 10 to 30 percent moisture," says FDA's Heinz Eiermann, director of the division of colors and cosmetics. "Near or below 10 percent, the stratum corneum [the outermost layer of skin] becomes dry and brittle. If repeated use of soap and water leach out too much of the moisturizing material, the skin cannot retain sufficient moisture and becomes dry, particularly in an environment with low relative humidity.

"However, the dry skin syndrome is not permanent because of the normal 20- to 25-day cell turnover. New stratum corneum cells are constantly being formed and the moisturizing material replenished."

When it is time to wash, both Kligman and Sanders recommend a mild soap followed by a moisturizer if needed. While many dermatologists tell patients that applying the moisturizer to damp skin will improve the moisturizer's effectiveness, Kligman says there is no evidence to support this. However, he said it doesn't seem to cause any harm, either.

The advice against washing too much applies to people with oily skin and acne as well as those with dry skin. "There is no evidence whatever that lack of washing worsens acne nor that frequent cleaning is helpful," Kligman said in his book *Acne, Morphogenesis and Treatment*. (See "Stubborn and Vexing, That's Acne" in the May 1980 *FDA Consumer*.)

"We no longer wash to get clean," said Kligman. "We wash to be refreshed. You won't damage the skin by never washing."

Other steps for good skin care include:

- Use a sunscreen. The strength of the sunscreen and how often it should be used depend on many factors, including skin color—fair skin requires a stronger sunscreen applied more often than darker skin—and geographical location—the sun's rays are strongest near the equator.
- To relieve dry skin, increase the humidity in the air if you live in a dry climate or if you spend the winter months in dry, overheated homes and offices. While humidifiers are the best way to increase humidity, house plants (which should be sprayed with water from time to time) and a pot of water on the radiator can help, too. ■

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effectiveness. Some commonly used humectants include urea, glycerin, pyrollidone, carboxylic acid, lactic acid, and propylene glycol. Vitamins, minerals and organic substances such as elastin, deoxyribonucleic acid, and ribonucleic acid didn't improve effectiveness either.

Despite many claims, collagen-based cosmetics offer no benefits beyond softening and moisturizing the skin. (Collagen, a protein, is the chief constituent of skin, connective tissue and bone. Most of the collagen used in cosmetics comes from cows.) Collagen's molecules are too large to get past the skin's outermost layer. However, collagen *injections*, done by a physician, can smooth out wrinkles (see "The Collagen Connection" in the June 1985 *FDA Consumer*).

Lotions and creams made with more oil than water always moisturize better than ones made with more water than oil. Of course, the ones with less oil are less messy and feel better, especially ones that promise "no greasy feeling" or that they are "absorbed quickly." The University of Pennsylvania study concluded that "a boon to all sufferers from dry skin would be a product with the efficacy of petrolatum and the hedonic-aesthetic properties of a light oil-in-water cream."

Studies on alleviating dry skin are rare. According to the University of Pennsylvania study, "the ordinary forms of dry skin, sometimes disdainfully called 'cosmetic dry skin,' do not enjoy high status in the medical establishment."

While some moisturizers can alleviate the symptoms of dry skin, there aren't any products for sale anywhere—from the pharmacy to the fanciest department store—that will actually get rid of wrinkles.

So why would anyone pay the high prices some companies charge for products that do nothing more than a jar of petroleum jelly can do, and sometimes less?

"Cosmetics are fashion products," explains Heinz Eiermann, director of FDA's division of colors and cosmetics. For some people, how the product feels and how it is absorbed is just as important as how well it works, he says. Even the packaging and the availability of salespeople may be an influencing factor, he believes. But he adds that, "There is absolutely no correlation between price and the quality of the product."

And, at least for now, there's no way to get rid of that wrinkle. ■

*Dori Stehlin is a member of FDA's public affairs staff.*

## SUBMISSION FOR THE RECORD

Page: 18

Line: 392

COMMITTEE ON SMALL BUSINESS

SUBCOMMITTEE ON REGULATIONS AND BUSINESS OPPORTUNITIES

HOUSE OF REPRESENTATIVES

SEPTEMBER 15, 1988

REQUEST: None --- Dr. Young offered for the record a chronology of significant regulations that FDA has promulgated.

SUBMISSION: Two charts: one of regulations which require warning statements, and the other, of regulations for prohibitions and restrictions of cosmetic ingredients.

## CHRONOLOGY OF REGULATIONS FOR SPECIFIC COSMETICS SINCE 1938

### PART I PROHIBITIONS AND RESTRICTIONS

| | |
|---|---|
| FEBRUARY 14, 1968 | FDA PROHIBITED THE FURTHER USE OF BITHIONOL BECAUSE OF ITS LIKELIHOOD OF CAUSING PHOTOCONTACT SENSITIZATION (21 CFR 700.11). |
| SEPTEMBER 27, 1972 | BECAUSE OF THE NEUROTOXIC EFFECTS AND ABILITY TO PENETRATE HUMAN SKIN OF HEXACHLOROPHENE (HCP), FDA RULED THAT IT MAY ONLY BE USED WHEN AN ALTERNATIVE PRESERVATIVE HAS NOT BEEN SHOWN TO BE AS EFFECTIVE. THE CONCENTRATION IS LIMITED AND IT MAY NOT BE USED IN COSMETICS WHICH IN NORMAL USE MAY BE APPLIED TO MUCOUS MEMBRANE (21 CFR 150.150). |
| JANUARY 5, 1973 | FDA RESTRICTED THE USE OF MERCURY COMPOUNDS AS COSMETIC INGREDIENTS TO EYE AREA COSMETICS AT LIMITED CONCENTRATIONS BECAUSE THESE COMPOUNDS ARE READILY ABSORBED THROUGH THE SKIN AND MAY CAUSE ALLERGIC REACTIONS, SKIN IRRITATION OR NEUROTOXIC MANIFESTATIONS (21 CFR 700.13). |
| AUGUST 26, 1974 | FDA PROHIBITED THE FURTHER USE OF VINYL CHLORIDE AS AN INGREDIENT OF AEROSOL PRODUCTS BECAUSE OF ITS CARCINOGENIC EFFECT IN HUMANS AND ANIMALS (21 CFR 700.14). |
| OCTOBER 30, 1975 | FDA PROHIBITED THE FURTHER USE OF HALOGENATED SALICYLANILIDES (di-, tri- metabromsalan and tetrachlorosalicylanilide) BECAUSE OF THEIR POTENTIAL OF CAUSING PHOTOCONTACT SENSITIZATION (21 CRF 700.15). |
| AUGUST 16, 1977 | FDA PROHIBITED THE FURTHER USE OF AEROSOL COSMETIC PRODUCTS CONTAINING ZIRCONIUM BECAUSE OF TOXIC EFFECT ON LUNGS, INCLUDING GRANULOMAS (21 CFR 700.16). |
| JUNE 29, 1976 | FDA PROHIBITED THE FURTHER USE OF CHLOROFORM BECAUSE OF ITS ANIMAL CARCINOGENICITY AND LIKELY HAZARD TO HUMAN HEALTH (21 CFR 700.18). |
| MARCH 17,1978 | FDA PROHIBITED THE FURTHER USE OF CHLOROFLUOROCARBONS IN COSMETIC PRODUCTS AS PROPELLANTS IN SELF-PRESSURIZED CONTAINERS INTENDED FOR DOMESTIC CONSUMPTION (21 CFR 700.23 AND 2.125). |
| DECEMBER 18, 1985 | FDA PROPOSED TO BAN THE USE OF METHYLENE CHLORIDE AS AN INGREDIENT IN ALL COSMETICS BECAUSE OF STUDIES INDICATING INHALATION OF THE CHEMICAL CAUSES CANCER IN LABORATORY ANIMALS, AND MAY BE CARCINOGENIC IN HUMANS. |

## CHRONOLOGY OF REGULATIONS FOR SPECIFIC COSMETICS SINCE 1938

PART II WARNING STATEMENTS

| | |
|---|---|
| MARCH 3, 1975 | FDA ESTABLISHED WARNING STATEMENT REGULATIONS WHICH MUST BE CONSPICUOUSLY DISPLAYED ON THE LABEL (21 CFR 740.1). |
| MARCH 3, 1975 | FDA ESTABLISHED THE LABELING OF COSMETIC PRODUCTS FOR WHICH ADEQUATE SUBSTANTIATION OF SAFETY HAS NOT BEEN OBTAINED. EACH INGREDIENT AND EACH FINISHED PRODUCT MUST BE ADEQUATELY SUBSTANTIATED FOR SAFETY PRIOR TO MAKETING. ANY SUCH INGREDIENT OR PRODUCT WHOSE SAFETY IS NOT SUBSTANTIATED PRIOR TO MARKETING IS MISBRANDED UNLESS IT CONTAINS THE FOLLOWING CONSPICUOUS STATEMENT ON THE PRINCIPAL DISPLAY PLANEL: **WARNING - THE SAFETY OF THIS PRODUCT HAS NOT BEEN DETERMINED (21 CFR 740.10).** |
| MARCH 3, 1975 | FDA REQUIRED WARNINGS ON COSMETICS P ACKAGED IN SELF-PRESSURIZED CONTAINERS (21 CFR 740.11). |
| MARCH 3, 1975 | FDA REQUIRED WARNINGS ON PRODUCTS WHOSE LABELING STATES OR SUGGESTS THAT THE PRODUCT IS FOR USE IN THE FEMALE GENITAL AREA OR FOR USE ALL OVER THE BODY (21 CFR 740.12). |
| AUGUST 19, 1990 | FDA REQUIRES CHILDREN'S FOAMING DETERGENT BATH PRODUCT (BUBBLE BATH) AND ALL OTHER FOAMING DETERGENT BATH PRODUCTS NOT LABELED AS INTENDED FOR USE EXCLUSIVELY BY ADULTS, BEAR ADEQUATE DIRECTIONS FOR SAFE USE AND ALSO A CAUTION STATEMENT (21 CFR 740.17). |

ATTACHMENT

## SUMMARY OF PERTINENT DATA ON COSMETIC INDUSTRY PARTICIPATION IN THE VOLUNTARY COSMETIC REGISTRATION PROGRAM AS OF JULY 1988

| | (TOTAL) | (SUBTOTAL) | PERCENT OF |
|---|---|---|---|
| Establishment Registrations | 684 | | |
| Firms Registering Formulations | 1,008 | | |
| Filing and Amending Formulations since 1984 | | 144 | (14% of 1,008) |
| Filing Formulations since 1984 | | 382 | (38% of 1,008) |
| Filing Amendments since 1984 | | 333 | (33% of 1,008) |
| Never Filed Amendments | | 523 | (52% of 1,008) |
| Firms Filing Experiences Between 1984-1987 | 183 | | |
| Filing or Amending Formulations since 1984 | | 126 | (69% of 183) |
| Experiences Filed by Contract Manufacturers | | 36 | (29% of 126) |
| Filing and Amending Formulations since 1984 | | 72 | (39% of 183) |
| Filing Experiences but not Formulations | | 5 | ( 3% of 183) |
| Firms Filing Experiences for 1987 | 115 | | |
| Filing or Amending Formulations in 1986-1988 | | 88 | (76% of 115) |
| Experineces filed by Contract Manufacturers | | 25 | (28% of 88) |
| Filing and Amending Formulations in 1986-1988 | | 43 | (37% of 115)<br>( 4% of 1,008) |

# SUBMISSION FOR THE RECORD

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Line: 727

COMMITTEE ON SMALL BUSINESS
SUBCOMMITTEE ON REGULATIONS AND BUSINESS OPPORTUNITIES
HOUSE OF REPRESENTATIVES
SEPTEMBER 15, 1988

REQUEST: None. Dr. Young stated that FDA would submit for the record the number of cosmetic firms that are participating in the voluntary programs.

SUBMISSION: Data on industry participation in the voluntary registry.

## Status of Cosmetic Registration Activities
## July 1988

| | Filed | Estimated Total | Level of Participation |
|---|---|---|---|
| Establishment Registrations | | | |
| Voluntary Registrations | 684 | 2,000- 2,500 | 27 - 34% |
| From All Sources | 1,444 | 2,000- 2,500 | 58 - 72% |
| Firms Registering Experiences for 1987 | 115 | 4,000- 5,000 | 2.3 - 2.9% |
| and | | | |
| Amending or Filing Formulations since 1986 | 88 | 4,000- 5,000 | 1.8 - 2.2% |
| Amending and Filing Formulations since 1986 | 43 | 4,000- 5,000 | 0.9 - 1.1% |
| Firms Having Registered Product Formulations | 1,008 | 4,000- 5,000 | 20 - 25% |
| Product Formulations Currently Registered | 19,389 | 40,000-50,000 | 39 - 48% |

## SUBMISSION FOR THE RECORD

Page: 44/45

Line: 1043

COMMITTEE ON SMALL BUSINESS
SUBCOMMITTEE ON REGULATIONS AND BUSINESS OPPORTUNITIES
HOUSE OF REPRESENTATIVES
SEPTEMBER 15, 1988

REQUEST: FDA, in cooperation with the cosmetic industry, is to review the 884 cosmetic ingredients found in the NIOSH Registry of Toxic Effects of Chemical Substances (RTECS) and develop an outline to determine a priority process for the review of the chemicals that are most important.

SUBMISSION: Copy of FDA outline and a copy of a Memorandum of Meeting of October 11, 1988 with representatives of CTFA on this outline.

**DEPARTMENT OF HEALTH & HUMAN SERVICES** Public Health Service

Food and Drug Administration
Rockville MD 20857

Outline For A Review Of The 884 Chemicals
Listed In NIOSH's Registry of
Toxic Effects Of Chemical Substances (RTECS)
Which Have Been Identified As Being
Used As Cosmetic Ingredients.

The review process may consist of the following phases and the chemicals may be divided into the following groups:

(1) The chemical names of the 884 entries in the RTECS will be converted to the more readily recognizable cosmetic ingredient names. The chemicals not recognized as cosmetic ingredients by industry and government representatives will be deleted.

(2) The remaining chemicals will be reviewed to identify those substances that have been evaluated by one of the following:

(a) FDA or FDA appointed advisory review panels, such as color additives approved for use in food, drugs or cosmetics (21 CFR 74 et seq.), or such as over-the-counter drug ingredients (21 CFR 330 et seq.);

(b) The Cosmetic Ingredient Review (CIR) expert panel reviewing chemicals used as cosmetic ingredients; or

(c) The International Fragrance Association technical advisory committee for substances used in cosmetics as fragrance ingredients.

The data cited in the respective RTECS monographs would be reconciled with the findings of the Agency and industry reviews.

(3) The remaining chemicals, not previously reviewed by the Agency or expert panels for safe use in cosmetics or drugs, would be compared with the lists of approved food additives (21 CFR 172 et seq.) and the lists of food substances generally recognized as safe (GRAS) (21 CFR 182 et seq.). The food additives and GRAS substances would be reviewed for their topical and systemic safety under conditions of topical cosmetic uses.

(4) The remaining chemicals which have not been reviewed by FDA or an expert panel will be prioritized for review on the basis of:

(a) Their frequency of use in cosmetics;

(b) Their known or anticipated biological activity;

(c) The anticipated skin penetration;

(d) The likely uses of the cosmetics containing the chemicals;

(e) The concentrations used in cosmetic formulations; and,

(f) Their association with consumer complaints.

The data elements are weighted and added to calculate a priority score. The formula for calculating the priority score was developed by CIR in cooperation with FDA staff. It is currently being used for prioritizing cosmetic ingredients for the industry's review program. It has served well for that purpose.

This process, which is a continuation of ongoing Agency and industry efforts, will remain a dynamic one, in which new chemicals will be added for, or deleted from, consideration as appropriate.

# MEMORANDUM OF MEETING

Date: October 11, 1988

Place: Center for Food Safety and Applied Nutrition
Food and Drug Administration , Washington, DC

Participants:

Cosmetic, Toiletry and Fragrance Association (CTFA)

G. N. McEwen, Ph.D.
Anita Curry

FDA

Heinz J. Eiermann
John E. Bailey, Ph.D
John A. Wenninger
Division of Colors and Cosmetics
M. L. Richardson, Office of Legislative Affairs

Subject: Outline of Plan for Review of Cosmetic Ingredients listed in NIOSH's Registry of Toxic Effects of Chemical Substances.

The meeting was arranged in response to Congressman Wyden's request at the September 15, 1988, hearing on The Health Hazards of Common Cosmetics for development, in cooperation with the cosmetic industry, of an outline of a plan for review of cosmetic ingredients listed in NIOSH's Registry of Toxic Effects of Chemical Substances (RTECS).

A short review of the attendee's suggestions of the approaches that might be taken to respond to this request quickly demonstrated essential unanimity in thought. It was agreed that after conversion of the chemical names to cosmetic ingredient names and deletion of chemicals which are not used in cosmetics and those which have already been reviewed by the expert panel of the Cosmetic Ingredient Review, the remaining chemicals could be grouped into (1) chemicals approved as food additives or considered GRAS (generally recognized as safe), (2) chemicals approved as color additives for use in foods, drugs or cosmetics, (3) chemicals listed as drug ingredients in USAN (United States Adopted Names) dictionary, and (4) chemicals not listed in the aforementioned three groups. The group (4) chemicals may be prioritized on the basis of their frequency of use, biological activity, likely human exposure, and likely skin penetration, using the weighted formula to calculate a priority score as developed in cooperation with the CIR staff.

On other matters, the CTFA representatives requested a listing by product category of the numbers of units of cosmetics sold in 1987 by the 115 firms participating in the program of voluntary registration of cosmetic product experiences. The CTFA representatives wanted that list as a basis for exploring changes in the registration process to stimulate greater industry participation. The information will be made available to the extent that the disclosure will not violate the confidentiality provisions of 21 CFR 730.7.

## SUBMISSION FOR THE RECORD

Page: 51

Line: 1202

COMMITTEE ON SMALL BUSINESS
SUBCOMMITTEE ON REGULATIONS AND BUSINESS OPPORTUNITIES
HOUSE OF REPRESENTATIVES
SEPTEMBER 15, 1988

REQUEST: None. Dr. Young stated that he would provide for the record the number of detentions of imported cosmetics.

SUBMISSION: The number of detentions of imported cosmetics:

| | | |
|---|---|---|
| FY-87 | 567 | |
| FY-88 | 477 | For the time period beginning October 1, 1987 through May 1, 1988, |

## DETENTIONS OF IMPORTED COSMETICS

| | |
|---|---|
| FY-87 | 567 DETENTIONS |
| FY-88 | 477 DETENTIONS FOR THE TIME PERIOD BEGINNING OCTOBER 1, 1987 THROUGH MAY 1, 1988 |

# SUBMISSION FOR THE RECORD

Page: 54

Line: 1280

COMMITTEE ON SMALL BUSINESS
SUBCOMMITTEE ON REGULATIONS AND BUSINESS OPPORTUNITIES
HOUSE OF REPRESENTATIVES
SEPTEMBER 15, 1988

REQUEST: Mr. Price asked Dr. Young for the number of seizures FDA has made on cosmetic products.

SUBMISSION: FDA provided the number of seizures to Mr. Wyden in a letter dated August 17, 1988 that was in response to a request for information on cosmetics:

FY-87: 5 seizures

# NUMBER OF COSMETIC PRODUCT SEIZURES MADE IN 1987

FDA PROVIDED THIS DATA, THE NUMBER OF SEIZURES OF COSMETIC PRODUCTS, IN A LETTER TO THE CHAIRMAN ON AUGUST 17, 1988..

IN FY-87 THERE WERE 5 COSMETIC PRODUCT SEIZURES.

STATEMENT OF
CHARLES ADKINS
DIRECTOR OF HEALTH STANDARDS PROGRAMS
OCCUPATIONAL SAFETY AND HEALTH ADMINISTRATION
U.S. DEPARTMENT OF LABOR
BEFORE THE
SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES
COMMITTEE ON SMALL BUSINESS
U.S. HOUSE OF REPRESENTATIVES

September 15, 1988

Mr. Chairman and Members of the Subcommittee:

Thank you for the opportunity to testify today. I am Charles Adkins, Director of Health Standards Programs for the Occupational Safety and Health Administration (OSHA). With me at the table is Jennifer Silk, an OSHA health scientist. Our agency shares this subcommittee's concern over potential health hazards to employees exposed to cosmetics products at work. We appreciate the information you have brought to light on this issue in the course of these hearings.

It may be useful if I begin by describing OSHA's overall responsibility for workplace safety and health. OSHA was established pursuant to the Occupational Safety and Health Act of 1970 (OSH Act). This statute grants the agency broad authority to promote the safety and health of employees on the job. OSHA's authority extends to private sector employers with one or more employees. The OSH Act authorizes OSHA to establish occupational safety and health standards, conduct inspections to enforce the standards, issue citations and propose monetary penalties for violations of the law, require employers to abate hazards, provide for training and education, and encourage employer-employee cooperative programs to reduce workplace hazards. Thus, OSHA has a wide range of tools to use in preventing occupational hazards.

In addition to the Federal program, twenty States and two jurisdictions conduct their own comprehensive, federally approved, safety and health programs, or "plans." Two other states -- Connecticut and New York -- operate partial plans covering only state and local government employees. The States maintain inspection forces and operate safety and health programs that are required to be at least as effective as the Federal program.

There are a number of standards which OSHA uses to control hazards in hairdressing establishments or other workplaces where employees may be exposed to cosmetic products. OSHA may use section 5(a)(1) of the OSH Act -- the "General Duty Clause" -- which requires employers to furnish a place of employment free from serious, recognized hazards. The agency currently enforces exposure limits for more than 400 air contaminants. A number of these substances, such as ammonia and benzoyl peroxide, are found in cosmetic products.

The agency also enforces twenty-four comprehensive standards for chemical substances, including formaldehyde, ethylene oxide, asbestos, and vinyl chloride. Some of these substances, such as formaldehyde, are used extensively in the cosmetics industry. These comprehensive standards include provisions for exposure monitoring, medical surveillance, engineering controls, education, training, and recordkeeping.

We have recognized for some time that the substance-by-substance approach which OSHA has used in the past is not sufficient to address the thousands of chemical hazards in the nation's workplaces. In 1983, OSHA took a dramatic step forward in addressing these hazards when it issued a broad Hazard Communication Standard which covered more than 500,000 chemical products and substances found in the nation's workplaces. This regulation provides workers exposed to hazardous chemicals with the right to know the identities and hazards of chemical substances, as well as to know the appropriate means to protect themselves from adverse health effects.

Any chemical that poses either a physical hazard (such as flammability) or a health hazard (such as causing damage to the skin or eyes) is covered by the rule. Employers are required to prepare a simple written program with a list of the chemicals in the workplace, to maintain labels on containers, obtain and maintain material safety data sheets for the hazardous products, and train potentially exposed workers. The Hazard Communication Standard (HCS) is dynamic in nature; as new chemicals are introduced into the workplace and new information about existing chemicals becomes available, producers must update the information they provide to their customers, and employers must update their hazard communication programs.

Since 1980, when OSHA first published a hazard communication, or labeling proposal as it was then known, the intent was to focus the new, landmark regulation on the industrial sectors where illness and injuries from chemical exposures were most prevalent. The standard, as issued in 1983, applied to the manufacturing sector only. Employers in the manufacturing sector were given two and a half years (until May 25, 1986) to come into compliance with all provisions of the standard since the rule represented a dramatic departure from the usual way of addressing chemical hazards. The standard had been in effect only little more than a year when, in August 1987, OSHA revised it to cover _all_ workplaces, including beauty salons, barber shops and other establishments where cosmetics are used.

The standard requires that all chemical manufacturers and importers review scientific evidence on the hazards of the chemicals which they produce or import. They must then inform their employees, as well as employers to whom they ship their products, about the hazards. Manufacturers and importers must ensure that each container of a hazardous chemical is labeled, tagged or marked with the identity of the chemical, appropriate hazard warnings and the name and address of the manufacturer or other responsible party. The label or tag must be retained on the container when it is used in the workplace. Labels must be legible and they must be prominently displayed.

Manufacturers, formulators and importers are also required to develop a Material Safety Data Sheet (MSDS) for each hazardous chemical or substance which they produce or import. The MSDS must be provided to the "downstream" distributor or user of the product at the time of initial shipment. Each MSDS must include information concerning the specific chemical identity of the hazardous substance and the common names of the substance. Information must also be provided about the physical and chemical characteristics of the substances, any known acute or chronic health effects, exposure limits, evidence of carcinogenicity, emergency and first aid procedures, and the identification of the organization responsible for preparing the MSDS. Any questions concerning the information can then be referred to that organization. Employers are required to ensure that copies of the MSDS's for chemicals in the workplaces are readily accessible to employees during each workshift. Since September 23, 1987, manufacturers, importers and distributors have been required to send MSDS's for hazardous chemicals which are supplied to "downstream" employers in all sectors, including hair-dressing establishments and other workplaces where cosmetics are used.

The standard also contains requirements for educating employees. Employers are required to establish a training and information program for all workers exposed to hazardous chemicals. The training and information must be provided at the time of initial assignment and whenever a new hazard is introduced into the work area. Employees must receive training on how to read and interpret information on labels and the MSDS; they must be told about methods of detecting the presence of chemicals. OSHA is enforcing this standard vigorously. In Fiscal Year 1987 the agency cited 19,674 violations of the Hazard Communication rule.

OSHA's enforcement of existing permissible exposure limits will be dramatically improved by its current project to update and revise the limits. Evidence indicates that many of the approximately 400 exposure limits that were adopted by OSHA at its inception are no longer fully protective of workers. Therefore, OSHA has recently issued a proposal to establish lower exposure limits for more than 200 of these chemicals and establish exposure limits for the first time for another 168 substances. At completion, OSHA will directly regulate almost 600 air contaminants or toxic substances. This rulemaking effort, which is scheduled for completion in December, will increase protection for 3.7 million employees in a variety of industries, including cosmetics and beauty products manufacturing and service establishments. The project revises exposure limits for hundreds of chemicals at one time. By addressing all of these substances in a single rulemaking OSHA is attempting to accelerate its efforts to protect workers from toxic chemicals. While the "PEL Project," as it is termed, will not replace comprehensive regulations, it is an important step for OSHA and for American workers.

One important way OSHA assists employers, particularly small business employers, in protecting their employees is through the on-site consultation program. State consultants, funded by OSHA, offer free consultation to employers upon request. They provide guidance on what constitutes an effective occupational safety and health program and offer advice on recognizing and eliminating hazards in the individual workplace. All states offer consultation services to employers with small businesses, who often lack the resources to hire occupational safety and health expertise. Since 1975, state consultants have visited more than 270,000 workplaces. More than 1.5 million hazards have been addressed under this program.

I wish to emphasize that OSHA has put in place the mechanisms and requirements to protect employees in the cosmetics industry. We have set numerous standards as well as substance-specific exposure limits and are improving them. The Hazard Communication Standard provides employees with information to recognize and protect themselves against hazards. OSHA offers assistance to employers through its consultation and education programs. If these mechanisms are not sufficient, employees may submit a formal complaint to OSHA when confronted with a serious work hazard. We believe that the multi-facted effort which I have described is protecting workers in the cosmetic industry.

Mr. Chairman, that concludes my statement on OSHA's efforts to protect employees exposed to cosmetic products. I will be happy to answer any questions.

# TESTIMONY OF

# WILLIAM MACLEOD

ON BEHALF OF THE
FEDERAL TRADE COMMISSION

Before

HOUSE COMMITTEE ON SMALL BUSINESS
SUBCOMMITTEE ON REGULATION
AND BUSINESS OPPORTUNITIES

Washington, D.C.

September 15, 1988

Thank you for the opportunity to appear before you today and discuss the Federal Trade Commission's role in the regulation of cosmetic advertising.[1]

## I. FTC AUTHORITY

The Federal Trade Commission is an agency with broad responsibility for policing "unfair or deceptive acts or practices."[2] In addition to the Federal Trade Commission Act's general prohibition of unfair and deceptive acts or practices, the Act contains statutory provisions that deal specifically with food, drugs, cosmetics, and medical devices. Section 12 of the FTC Act prohibits "false advertisements" for food, drugs, devices and cosmetics. Section 15 of the FTC Act defines a false advertisement to mean one which is misleading in a material respect. Under Section 15(a)(1), an advertisement may also be found to be "false" if it fails to reveal facts which are material in light of what is said in the ad, or which are material with respect to consequences which may result from use of the product under conditions prescribed in the ad or under conditions that are customary and usual.

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[1] Although the Subcommittee's September 1, 1988 letter asks for information concerning the FTC's role in regulating cosmetic labels, as explained on pages 2-3 of this testimony the Commission's primary responsibility is for the advertising of cosmetics, not for labeling.

[2] 15 U.S.C. § 45 _et seq_. (1988 Supp.).

## II. LIAISON WITH FDA

The FTC and the Food and Drug Administration ("FDA"), have overlapping jurisdiction over the advertising and labeling of food, drugs, cosmetics and devices.[3] The two agencies have, therefore, established a liaison agreement which allocates responsibilities between them. The agreement has resulted in a long-standing degree of cooperation between the agencies, each having primary jurisdiction over areas in which it has developed expertise. The agreement basically provides that, except for prescription drug advertising, the FTC has primary responsibility to regulate advertising of food, drugs, devices and cosmetics, and the FDA has primary responsibility for preventing misbranding or mislabeling of food, drugs, devices, and cosmetics. Under the agreement, the FTC and FDA will avoid initiating separate proceedings against the same party except when such action will be in the public interest. To avoid duplication or inconsistent regulatory decisions, liaison activity is required where the same claims appear in both advertising and labeling, and where the same material could be either "labeling" or "advertising."[4]

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[3] The Subcommittee's September 1, 1988, letter refers to possible FTC jurisdiction over cosmetics under the Fair Packaging and Labeling Act, 15 U.S.C. § 1451. Under Section 7(a) of that Act, the Food and Drug Administration is given jurisdiction with respect to foods, drugs, devices and cosmetics, 15 U.S.C. § 1456.

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[4] Updated FTC-FDA Liaison Agreement - Advertising Of Over-The-Counter Drugs, CCH TRADE REG. RPTS. § 9851 (1971).

Since the original version of this agreement became effective in 1954,[5] it has set the stage for close and continuing contact between the two agencies on a variety of issues, including the advertising and marketing of cosmetics.

## III. FTC'S APPROACH TO ADVERTISING REGULATION

As already noted, the FTC Act makes unlawful advertisements that are deceptive or unfair. Therefore, we view our mission as preventing the dissemination of false, unsubstantiated, or materially misleading advertising, or advertising that causes substantial and unavoidable consumer injury that is not balanced by benefits to consumers or to competition in general.

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[5] The agreement has been updated twice, most recently in 1971.

The FTC staff monitors national advertising in both print and broadcast media on a regular basis. In addition to our monitoring, both competitor and consumer complaints can be an important source of information concerning potentially deceptive, unfair or unsubstantiated claims. Finally, referrals from other government agencies such as the Food and Drug Administration and state and local consumer protection agencies often are another important source of leads. Investigations may be initiated by headquarters staff attorneys with approval of the associate director for advertising practices, or by Regional Office attorneys with approval of their regional director.

### A. Deception

In deciding whether an ad contains a particular deceptive claim, the Commission concerns itself with how consumers are likely to interpret the claims made in the ads. We examine claims in the context in which they appear and seek to determine the impression created by the advertisement viewed as a whole. Even a claim that is literally true may be deceptive if material information is omitted or if other parts of the advertisement create a misleading impression. In addition, although there are differences between the functions and purposes of labeling and advertising, the fact that a label is accurate will not cure a deceptive ad.

In deciding whether an advertisement warrants further investigation to determine whether there may be reason to believe it may be deceptive, the Commission staff also assess the extent of consumer injury.[6] For example, taking action to halt an alleged misrepresentation that may cause adverse health consequences to consumers is likely to take priority over addressing a deceptive claim that appears to involve relatively minor and purely economic injury. Similarly, if the product is inexpensive, we try to ascertain whether the claim can be evaluated by the consumer easily and without significant cost (for example, whether a particular deodorant is dry or a particular lipstick "smudge-proof"), or whether it is unlikely to be susceptible to assessment by the ordinary consumer or can be tested only at substantial cost (for example, whether a motor oil provides adequate protection for an automobile engine or whether a drug contains appropriate amounts or types of therapeutic ingredients).[7] In the market for relatively inexpensive, frequently purchased products, when claims can be readily verified, consumers often can regulate the accuracy of advertising through their decisions on whether or not to buy the product again.

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[6] The staff also considers whether industry self-regulation can resolve the issue without action by the government. Each of the major networks maintain a vigorous advertising clearance mechanism and the industry self-regulatory system, operated by the Better Business Bureau's National Advertising Division, has handled almost 300 cases involving cosmetics.

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[7] See Bristol-Myer Company, 85 F.T.C. 688, 746, 751-752 (1975).

Traditionally, cosmetic advertising has relied heavily on a combination of "puffery" and subjective claims, such as "makes you look or feel beautiful." For the most part, the Commission's advertising program has not focused on advertisements containing such claims. Instead, the Commission has concentrated its efforts on advertising for cosmetic products that include health or safety claims or that otherwise present a significant risk of physical injury when used.

While focusing on health and safety claims, the Commission also brings cases against claims posing primarily the risk of economic injury. Thus, for example, the FTC has brought actions against several marketers of cosmetic hair care products which falsely claimed they prevented or cured baldness.[8] Similarly, the Commission has initiated actions against individuals allegedly offering painless $750 to $1,500 "laser facelifts" which the Commission charged were ineffective.[9]

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[8] U.S. v. Braswell, Inc., et al., No. C81-55A (N.D. Ga. Sept. 14, 1983); FTC v. Intra-Medic Formulations, Inc., et al., (S.D. Fla. Feb. 28, 1986).

The Commission staff are also currently in litigation with the largest maker of high-frequency, tweezer-type hair removal devices, which is charged with making false and unsubstantiated advertising claims that its products could permanently remove hair. These devices are allegedly sold to beauty-salons for $4,000 and treatments of customers cost $10-$35 per treatment over several years' time.[10] This case is currently pending on appeal before the Commission.

More recently, the Commission staff also conducted investigations of "anti-aging" claims made by some cosmetic manufacturers. However, activity on these investigations was curtailed when FDA took industry-wide action in 1987. We are continuing to monitor advertising in this area and will initiate follow-up investigations where necessary.

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[9] See, Laser Toning Center, 102 F.T.C. 1319 (1983).

[10] Removatron International Corp., et al., D. 9200 (int. dec. July 15, 1987). Initial decision, appeal pending.

### B. Unfairness

As I said at the outset, advertising may be unlawful if it is deceptive. It may also violate the FTC Act if it is unfair.

As pointed out in the Companion Statement to the Commission's 1980 Policy Statement on Unfairness, the unfairness theory historically has been directed primarily at practices other than advertising (such as coercive sales practices).[11] Nonetheless, we have relied on it to challenge successfully restrictions on truthful advertising as well as advertising that raises significant health risks. For example, it served as an alternative basis for the Commission's early trade regulation rule requiring health warnings in cigarette advertising.[12]

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[11] See Companion Statement to Letter from Commission to Honorable Wendell H. Ford and John C. Danforth (December 17, 1980) ("Unfairness Policy Statement") at 3.

The primary criterion for determining whether an advertisement is unfair is consumer injury. In considering whether an advertisement is unfair, the Commission looks to whether the advertisement is likely to result in consumer injury that:

(1) Is substantial;

(2) Is not outweighed by countervailing benefits to consumers or competition; and

(3) Is an injury that consumers themselves could not reasonably have avoided.[13]

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[12] The Commission's current appropriation prohibits expenditures of Commission funds for the purpose of initiating any rulemaking prohibiting or regulating commercial advertising based on the Commission's unfairness jurisdiction.

[13] Int'l. Harvester Co., 104 F.T.C. 949, 1061 (1984).

## C. Ad Substantiation

Another important part of the Commission's effort in the area of cosmetic advertising is its advertising substantiation program. Under this program, it is unfair and deceptive for an advertiser to make an objective product claim, unless the advertiser has a reasonable basis for believing the claim to be true at the time it is made.[14]

The key question in evaluating claims in terms of ad substantiation doctrine is, how much substantiation is enough? As the Commission's policy statement on ad substantiation makes clear, and consistent with recent court decisions upholding the Commission's authority to require substantiation,[15] the level of substantiation required for any given claims will vary depending on the type of claim made.

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[14] See also, FTC Policy Statement Regarding Advertising Substantiation, 49 Fed. Reg. 30999-31001 (August 2, 1984); Thompson Medical Company, 104 F.T.C. 648, 839-842 (1984), aff'd, 791 F.2d 189 (D.C. Cir. 1986), cert. denied, 107 S.Ct. 1289 (1987).

[15] See, e.g., Thompson Medical Co., supra, 791 F.2d 194-95.

As a general rule, all claims must be supported by the level of substantiation they communicate to the reader or listener. For example, where a claim expressly promises that it is supported by properly conducted clinical tests, it must, in fact, be supported by properly conducted clinical tests.

Similarly, if the ad claims that the product is supported by the findings of a scientific report, it must, in fact, be supported by such a report. In addition, if the ad implies a higher level of substantiation than it _expressly_ claims, the actual substantiation relied on must support the higher standard.

If the advertisement does not expressly or impliedly state a particular level of support for its claims, the Commission looks at whether the advertiser has a "reasonable basis" for the claims. For any given claim, what constitutes a "reasonable basis" depends on an analysis of factors that have become well established in Commission case law. These factors are:

(1) The type of claim;
(2) The type of product;
(3) The benefits of a truthful claim;
(4) The consequences of a false claim;
(5) The cost of developing substantiation for the claim;
(6) The amount of substantiation experts in the field believe is reasonable.

In sum, the six criteria are part of a balancing analysis that enables the FTC to consider not only the likelihood that a particular claim is true, but also to weigh the likely consequences of allowing claims based on the available substantiation.

Under this flexible approach, the required level of substantiation rises with the potential for consumer injury should the claim turn out to be false. For example, where the particular product claim raises concerns about possible injury to the health or safety of consumers or will be difficult or impossible for consumers to assess for themselves, the FTC requires a relatively higher level of substantiation.[16]

Investigations of a company's advertising substantiation normally begin with a letter to the company in which the staff sets out the claims that it believes have been made by the ad and asks for substantiation for these claims. If the company refuses to comply with these requests, the staff may request authorization from the Commission to issue compulsory process requiring production of such material. As a practical matter, however, because it is in the company's interest to demonstrate that its claims are supported, resort to compulsory process in advertising substantiation cases has been relatively rare.

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[16] Thompson Medical Co., supra, 104 F.T.C. at 822.

## IV. SHARING DATA WITH FDA

The Subcommittee's September 1, 1988 letter specifically asks about the Commission's ability to share date obtained in law enforcement investigations with FDA.

When proprietary data supporting the company's claims is obtained, distribution is limited to Federal Trade Commission employees.[17] FDA staff members and outside experts may be retained as Commission consultants and are required to sign nondisclosure affidavits before they can be given this information to review.[18] In addition, under the FTC Act, the Commission may provide confidential information to other federal agencies for law enforcement purposes.[19] Before such information may be disclosed, the agency must submit a written request to the

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[17] 15 U.S.C. 57b-2(b)(3)(C) (1988 supp.); 16 C.F.R. § 4.10(a)(8) & (9); see also 15 U.S.C. § 57b-2(F) (1988 Supp.).

[18] 16 C.F.R. § 4.10(d).

[19] 15 U.S.C. §§ 46(f) and 57b-2(b)(6).

FTC certifying that the information will be maintained in confidence and used only for official law enforcement purposes. The certificate must also describe the nature of the law enforcement activity and the anticipated relevance of the information to that activity.[20]

## V. PAST COMMISSION CASES

Most of the cosmetic advertising cases the Commission has brought in the past have involved products or claims for which there were underlying safety concerns.[21] For example, in 1975 the FTC entered an order which required a cosmetic manufacturer to cease advertising and packaging "Dark Eyes Lash And Brow Tint" without a warning to consumers that the product can cause severe pain to the eye for a substantial period of time.[22]

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[20] 16 C.F.R. § 4.11(c).

[21] Cases involving primarily economic injury are discussed in Section III A, above.

Similarly, in 1975, the FTC also took action to prevent promoters of chemical skin peeling processes from misrepresenting that an inherently dangerous treatment to remove facial wrinkles and blemishes was safe.[23]

The FTC also challenged the safety claims of a manufacturer of facial depilatory and beard removal products in 1975. The FTC found that the products contained chemicals which can cause burns, rashes, and other skin irritations for a substantial number of users.[24]

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[22] C.E.B. Products, Inc., et. al., 85 F.T.C. 565, 569, 573 (1975). (The potentially painful ingredient in this cosmetic was silver nitrate or silver sulfate.)

[23] See e.g., Miriam Maschek, Inc., et al., 85 F.T.C. 536 (1975).

[24] Carson Products Co., et al., 86 F.T.C. 1079 (1975).

The FTC also took action on advertisements for a number of hair relaxer or straightener products marketed to black men and women in the late 1970's. These products contain strong chemical ingredients like ethylene glycol, acid, ammonium thioglycolate, and sodium or potassium hydroxide (lye). Such ingredients can irritate and injure eyes and skin, cause hair damage and even cause hair loss. The FTC ordered warnings in advertising and specific directions for use for products sold by different companies.[25] Recent monitoring activity indicates that almost all hair relaxers and straighteners bear some variation of the warnings required by FTC orders, even for products offered by companies not under order.

Similarly, in the late 1970's and early 1980's the Commission initiated a number of investigations of products that made allegedly unsubstantiated claims about their ability to cure or prevent acne. The FTC obtained consent orders against marketers prohibiting them from making such claims in the future without a reasonable basis. These products, while not raising direct safety-related claims, were making claims concerning a significant health issue.[26]

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[25] Lustrasilk Corporation of America, Inc., et al., 87 F.T.C. 145 (1976); The Perma-Strate Company, et al., 87 F.T.C. 155 (1976); Soft & Sheen Company, Inc., et al., 87 F.T.C. 164 (1976); Johnson Products Company, Inc., et al., 87 F.T.C. 206 (1976); Revlon, Inc., et al., 89 F.T.C. 1 (1977).

More recently, the FTC obtained consent orders in 1988 from two major firms selling artificial tanning equipment. The Commission charged that companies claimed that their products were safe, could be used without eye protection, and did not pose some risks associated with sun damage -- i.e., skin damage, skin aging or skin cancer, while providing the cosmetic effects of a suntan. The FTC alleged that there were potentially harmful side-effects associated with exposure to these machines. The FTC prohibited these claims and required affirmative disclosures in all ads and promotional materials that make safety-related claims, directing consumers' attention to the mandatory FDA warning label found on every tanning machine.[27] In addition, the Commission will be issuing a consumer fact sheet which advises consumers on the hazards associated with tanning, whether by machine or the sun.

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[26] San-Mar Laboratories, Inc., et al., 95 F.T.C. 236 (1980); Harvey Glass, M.D., 95 F.T.C. 246 (1980); Karr Preventative Medical Products, Inc., et al.; 94 F.T.C. 1080 (1979); Cooga Mooga, Inc., et al.; 92 F.T.C. 310 (1978), modified, 98 F.T.C. 814 (1981); Savoy Drug & Chemical Company, 86 F.T.C. 957 (1975); American Image Corporation, et al.; 87 F.T.C. 174 (1976).

## VI. CURRENT INVESTIGATIONS INVOLVING COSMETIC CLAIMS

The Subcommittee has requested information concerning the number of current investigations being conducted concerning cosmetic claims. There are approximately fifteen such investigations. With respect to the anti-aging creams specifically, the Commission has recently supplied the

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[27] Sun Industries, Inc., No. C-3230 (May 13, 1988); The Silver Group, Inc., No. C-3225 (April 13, 1988). (1988).

Subcommittee with information concerning its current investigations. We would be happy to submit any further information the Subcommittee determines is necessary concerning these investigations.

I hope this has given you a useful summary of the Commission's approach to cosmetic claims. I appreciate the opportunity to appear before this Subcommittee.

UNITED STATES OF AMERICA
FEDERAL TRADE COMMISSION
WASHINGTON, D.C. 20580

BUREAU OF
CONSUMER PROTECTION

*October 21, 1988*

The Honorable Ron Wyden
Chairman, Subcommittee on Regulation
and Business Opportunities
Committee on Small Business
U.S. House of Representatives
Washington, D.C. 20515

Dear Chairman Wyden:

Thank you very much for the opportunity to appear before your Subcommittee on September 15, 1988, in regard to the Federal Trade Commission's activities regarding the safety of cosmetic products. At the hearing, you asked me to provide further information for the record.

Some of the information responsive to your first inquiry is nonpublic information. Although nonpublic, this information is not exempt from public disclosure under the Freedom of Information Act ("FOIA"), 5 U.S.C. § 552. Accordingly, the Commission has authorized me to provide this information to you without requesting that it be kept confidential.

1. **Provide a list of contacts within the last two years between the FTC and the FDA in which you shared information about safety issues applicable to cosmetics:**

As I mentioned in my testimony, the Commission has a longstanding liaison agreement with the FDA. Generally, contacts between the agencies are primarily of an informal and ongoing nature between staff members. Contact has been initiated by the FTC to obtain expert opinions, test data, and research from FDA scientific personnel, and to notify FDA of our cosmetic, investigation-related activities. FDA has often supplied us with expert advice, journal references, articles, FDA monographs, Federal Register notices, and more specifically, FDA regulatory letters and correspondence.

In the last two years, these contacts have been made to discuss the efficacy of certain cosmetic products including some "anti-aging" creams. With respect to your specific question concerning contacts about safety issues applicable to cosmetics, the FTC has consulted FDA only about hair straighteners.

The Commission staff recently reviewed advertising for hair straightener products. Since many of these products contain strong chemical ingredients, there exists a potential for consumer injury. In the mid-1970's the Commission brought several cases against manufacturers for failing to warn consumers about the dangers and required that manufacturers provide specific directions for their use. (*See*, our following response, 2 e.). Our recent monitoring activity indicated that almost all such products currently bear some variation of the warnings required by past FTC orders, even for products offered by companies not under order.

Safety issues related to products other than cosmetics have also been discussed with FDA during this same period. These products include suntanning equipment, drugs, cooking utensils and water filters. For example, we consulted extensively with FDA about the possible ill health effects caused by artificial suntanning equipment. Here again, the FTC relied on FDA's expertise in the safety area. FDA shared with us relevant technical data it had for such products. Subsequently, the FTC challenged two manufacturers' claims, and required them to cease making unqualified safety claims. In addition, the FTC required them to disclose in their ads in which safety or health benefit claims are made, a reference to and summary of the required FDA warning found on each piece of suntanning equipment. (*See*, our following response, 2 f.).

**2. Provide a list of cosmetic products, the safety of which prompted the FTC to take action to warn consumers:**

**a. Hair loss products:**

*U.S. v. Braswell, Inc.*, *et al.*, No. C81-55A (N.D. Ga 1983)

**b. Eyelash and eyebrow tint products:**

*C.E.B. Products, Inc.*, *et al.*, 85 F.T.C. 565 (1975)

**c. Chemical skin-peeling processes to remove wrinkles and blemishes:**

*Miriam Maschek, Inc.*, *et al.*, 85 F.T.C. 536 (1975)

**d. Facial depilatory and beard removal products:**

*Carson Products Co.*, *et al.*, 86 F.T.C. 1079 (1975)

**e. Hair straightener products:**

Lustrasilk Corp. of America, inc., et al., 87 F.T.C. 145 (1976);

The Perma-State Co., et al., 87 F.T.C. 155 (1976);

Soft & Sheen Co., Inc., et al., 87 F.T.C. 164 (1976);

Johnson Products Co., Inc., et al., 87 F.T.C. 206 (1976);

Revlon, Inc., et al., 89 F.T.C. 1 (1977).

**f. Suntanning equipment products:**

Silver Group, Inc., C-3225, iss. April 13, 1988;

Sun Industries, Inc., C-3230, iss. May 17, 1988.

I hope that this additional information will be helpful to you.

By direction of the Commission.

William C. MacLeod
Director
Bureau of Consumer Protection

COSMETIC INGREDIENT REVIEW

C I R

STATEMENT OF

ROBERT L. ELDER, SC.D.

DIRECTOR AND SCIENTIFIC COORDINATOR

COSMETIC INGREDIENT REVIEW (CIR)

BEFORE THE

SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

COMMITTEE ON SMALL BUSINESS

UNITED STATES HOUSE OF REPRESENTATIVES

WASHINGTON, D.C.

September 15, 1988

1110 Vermont Avenue NW Suite 810 WASHINGTON, DC 20005 202•331-0651

Mr. Chairman and members of the Committee, my name is Robert Elder. I have been the Director and Scientific Coordinator for over nine of the eleven years the Cosmetic Ingredient Review (CIR) has been in existence. Prior to this I was an Assistant Surgeon General in the United States Public Health Service and the Deputy Associate Commissioner for Science in the Food and Drug Administration.

## INTRODUCTION

The Cosmetic Ingredient Review (CIR) was established as a cosmetic industry self-regulation program in 1976 by the Cosmetic, Toiletry and Fragrance Association (CTFA). The program's sole mission is to evaluate the safety of ingredients used in cosmetic products. The cosmetic industry has conducted safety testing on individual ingredients and on cosmetic formulations for many years. Although some of this safety information has already been published, a significant portion has been kept in industry files and thus not available for public review. The CIR program is designed to bring together for public review and evaluation all of the worldwide data, both published and unpublished, on cosmetic ingredient safety.

The CIR program is modeled after the Food and Drug Administration (FDA) review of active ingredients in nonprescription drugs and in biological drugs. The written CIR Procedures, which are attached to this statement, describe the detailed requirements that must be followed in evaluating the safety of cosmetic ingredients. The program has four important fundamental characteristics.

1. The review is conducted in an open public manner where any individual may participate. All data, considered by CIR, including test methods, must be publicly available for review by any interested person. All of the records of CIR are publicly available. I would be pleased to submit any of these records to this Committee for review.

2. All decisions relating to the safety of cosmetic ingredients are made by an Expert Panel of seven independent academic scientists. The Expert Panel members must satisfy the same conflict of interest requirements as members of federal advisory committees.

3. The CIR program, including its staff and consultant scientists, is funded by, but kept separate from, the cosmetic industry. All reports issued by CIR are released to the public without prior CTFA or industry review.

4. Proof of the safety of a cosmetic ingredient must be documented through scientific evidence. A long history of safe use, or the lack of adverse information, is not sufficient to demonstrate proof of safety.

## CIR STEERING COMMITTEE AND THE EXPERT PANEL

The CIR Procedures establish two separate committees. The first is a Steering Committee, which provides policy advice and guidance to the overall CIR program. It is composed of two members from CTFA (the CTFA President and Vice-President for Science), one member from industry (the Chairman of the CTFA Science Advisory Committee) and two public members not from CTFA or the cosmetic industry (an academic toxicologist appointed by the American Society of Toxicology and an academic dermatologist appointed by the American Academy of Dermatology). The President of CTFA chairs this committee.

The second committee, the CIR Expert Panel, makes the decisions on cosmetic ingredient safety. The seven members of the Expert Panel are appointed by the Steering Committee from publicly nominated candidates. Nominations for the CIR Expert Panel may be made by anyone.

Each member of the Expert Panel must satisfy the same strict conflict of interest requirements that are imposed on special governmental employees who serve on advisory committees under federal law. They may not consult with, or have any financial interest in, any cosmetic manufacturer or supplier.

The CIR Expert Panel is charged with reviewing all of the available scientific data, both published and unpublished, prior to determining the safety of a cosmetic ingredient. The CIR Procedures specifically require that the Panel make one of three decisions with respect to the use of an ingredient in cosmetics:

1. Safe for use in cosmetic products, with or without limitations.

2. Unsafe for use in cosmetic products.

3. Insufficient data upon which to base a safety conclusion.

The Expert Panel is supported by a full time staff of eight: A Director, five scientific writers and analysts, and two administrative support personnel. None of these persons has ever worked for a cosmetic manufacturer or supplier.

In addition to the seven scientific experts, the CIR Expert Panel includes a consumer liaison, an industry liaison, and a contact person from the Food and Drug Administration. The consumer liaison is selected by the Consumer Federation of America. The industry liaison is selected by CTFA. The FDA contact person is selected by FDA. All three are invited to attend all CIR Expert Panel meetings.

The CIR Expert Panel normally meets five times per year, three times in a two-day public session and twice each year in a closed one-day report editing session. In CIR's eleven year history, there have been over 70 meetings. Only on two occasions has an individual Expert Panel member missed a meeting. The total overall budget of CIR is approximately $750,000 per year. CTFA provides the sole support for CIR.

The current CIR Expert Panel members are:

William O. Berndt, Ph.D., Chairman,
Vice Chancellor - Academic Affairs,
University of Nebraska Medical Center

Wilma F. Bergfeld, M.D., Head, Dermatopathology and
Staff Dermatologist, Cleveland Clinic Foundation

Roswell K. Boutwell, Ph.D., Professor of Oncology,
University of Wisconsin

William W. Carlton, D.V.M., Ph.D., Professor of
Veterinary Pathology and Toxicology,
Purdue University, School of Veterinary Medicine

Dietrich K. Hoffmann, Ph.D., Associate Director
and Chief, Division of Environmental Carcinogenesis,
American Health Foundation

Arnold L. Schroeter, M.D., Professor and Chairman
Dermatology, Wright State University School of Medicine

Ronald C. Shank, Ph.D., Professor and Director of
Environmental Toxicology,
University of California at Irvine

If the Committee desires, the curriculum vitae of the individual Expert Panel members will be submitted.

The Expert Panel evaluates the safety of each ingredient, or group of chemically-related ingredients, according to a priority list. The priority list establishes a time sequence for ingredient review. The first CIR priority list was released in 1977. It was re-evaluated in 1980 and 1984. Under the CIR Procedures, the Expert Panel may revise the order of this priority list at any time by adding new cosmetic ingredients, deleting materials no longer used, or giving a lower or higher ranking to ingredients.

The method used to establish priorities for review of cosmetic ingredients is critical to the entire CIR program. In 1977, the Steering Committee was faced with a problem similar to that faced by many federal government agencies who are involved with prioritizing a large number of chemicals for toxicological safety evaluation. After lengthy discussions with outside toxicological consultants, seven variables were selected for use in determining an ingredient's review priority: biological activity, frequency of use, area of application, frequency of application, known consumer complaints, use by sensitive subgroups, concentration of use). In 1983, FDA suggested that an additional factor should be used: an ingredient's ability to penetrate the skin. The Expert Panel concurred and skin penetration factor was included in the calculations used to establish the 1984 Priority List.

The eight factors used, and the percent contribution to the total score for each factor, are as follows:

Biological Activity. This is determined by reviewing the available toxicological data in the U.S. National Medical Library computer data base. A value is assigned based upon the apparent toxicity of the ingredient. If no data are available, a recommended value is assigned based upon the ingredient's chemical structure. In preparing the 1984

Priority List, over 20,000 abstracts were reviewed by the CIR staff. The maximum contribution to the total possible score for this factor is 29.4 percent.

Frequency of Use. The frequency of occurrence is based upon the data submitted to FDA by cosmetic manufacturers on ingredients used in cosmetic formulations. (21 C.F.R. Part 720.) This factor attempts to estimate the potential for public exposure and assumes that an ingredient that is used in a great number of formulations has the potential for exposing more people than one that is used less frequently. It is assumed that the data available approximate a sampling of the large and small cosmetic manufacturers. The 1984 Priority List includes all ingredients reported to FDA as being used in 20 or more formulations. The maximum contribution to the total possible score for this factor is 18.0 percent.

Estimate of Skin Penetration. A value is assigned, based upon actual absorption data or by using the ingredient's partition coefficient. If neither of these two factors is available, the possible penetration is estimated by the molecular weight. Lower molecular weight ingredients are given a higher score than those with high molecular weights. The maximum contribution to the total possible score for this factor is 25.5 percent.

Area of Skin Application. A value is assigned based upon the type of cosmetic product in which the ingredient is used. For example, a cosmetic formulation containing the ingredient that is designed for use in the area of the eye receives a higher value than one used on the fingernails. The maximum contribution to the total possible score for this factor is 22.0 percent.

Frequency of Application. This attempts to give recognition that repeated use, more than one time per day, may be of significance. Its overall contribution is low because many cosmetics are designed to remain in contact with the body surface throughout the day without reapplication. The maximum contribution to the total possible score for this factor is 1.0 percent.

Known Consumer Complaints. This is based upon the FDA records of complaints on cosmetic formulations which contain the ingredient. The contribution is none or all (0 or 1). It assumes that the specific ingredient being prioritized was the one causing the complaint. Because of the high range of uncertainty, the assigned weighting factor does not contribute significantly to the overall priority value. The maximum contribibtion to the total possible score for this factor is 1.0 percent.

Use by Sensitive Subgroups in the Population. This recognizes that some products are designed for infants or older people. Both groups may be more sensitive to cosmetic products than other population subgroups. Most cosmetic products are used by all groups. This variable (0 or 1) is assigned only to those formulations explicitly marketed for specific groups that may be more sensitive than the general population. Where equal scores occur for general use, this factor raises the final score and requires an earlier review. The maximum contribution to the total possible score for this factor is 1.0 percent.

Concentration of Use. This variable was introduced to give an increase in priority scoring for ingredients used at concentrations above twenty-five percent. It was intended to indicate concern for ingredients used at high concentrations on the body surfaces which, even if poorly absorbed, may be of safety significance because of the high concentration of use. The maximum percent contribution to the total possible score is 1.0 percent.

The biological activity, estimate of penetration, area of product application, and frequency of use can contribute up to 96 percent of the total possible score. The four lower weighted factors provide a mechanism for separating those ingredients that have the same score for the first four criteria. Beyond that, a recognition of these last four factors in the actual priority evaluation by the CIR Expert Panel is important. For example, a low concentration of use may be more significant for a preservative than a high level of use of an emulsifier. Yet a high concentration of use could be very significant in evaluating the possible absorption of an ingredient that is normally poorly absorbed. Therefore, obtaining the data for comparative purposes in setting review priorities between specific ingredients is quite useful.

The CIR staff priority calculations and the preliminary priority list of ingredients are first reviewed by the CIR Steering Committee. In its review of the 1977, 1980 and 1984 priority lists the Steering Committee did not recommend any deletion. In reviewing the 1980 evaluations, the Steering Committee requested that all preservatives that had been deferred because they are regulated by FDA for use in nonprescription drugs or in foods be added back into the priority list for review by the CIR Expert Panel.

After Steering Committee review, The proposed priority list is made publicly available for the 90-day public comment period. During this time period any individual may make recommendations or give opinions.

Following the 90-day public comment period, the priority list and all comments received are given to the CIR Expert Panel for their consideration and decision. Following the initial CIR Expert Panel approval of the entire list, the Expert Panel again reviews the list on an annual basis to reconfirm its opinion on the priority of review. Any Expert Panel member, at any time, may request the full Expert Panel for a change in the order of review. Only the CIR Expert Panel may change the order of ingredient review or add a new ingredient. This is done without approval by the Steering Committee or CTFA. To date, changes in the order of priority have been made only for an increased weighting for biological activity. For example, at the request of an Expert Panel member the Expert Panel agreed to raise the priority for review of morpholine because of its potentital role in producing nitrosamines.

A chemical supplier may not say that any reviewed ingredient has been "approved by CIR". Nonetheless, it is apparent that there is a market advantage for ingredients judged to be safe by CIR.

Many cosmetic ingredients are already approved for use as an ingredient in, or associated with, the manufacture of foods and drugs. To minimize duplicaiton of effort, the CIR Procedures permit the Expert Panel to defer, but not exempt from review, those ingredients that are subject to other existing FDA safety reviews. Thus, nonprescription drug ingredients, food flavors, GRAS (generally recognized as safe) food ingredients, food additives, and ingredients approved in new drug applications (NDA), have a lower priority for review. All substances that are subject to a final regulation by FDA are excluded from review. For example, all color additives are excluded because their safety is required to be determined by FDA under Section 706 of the Federal Food, Drug, and Cosmetic Act. Fragrance ingredients are excluded because they are the subject of a separate industry safety evaluation conducted by the Research Institute for Fragrance Materials (RIFM).

## The Number of Cosmetic Ingredients Actually in Use in the U.S.

The CTFA Ingredient Dictionary currently lists 5000 nonfragrance ingredients. These are ingredients that are offered for use by the cosmetic industry. Many are not used in a cosmetic at any given time. It is estimated that about 2300 of these nonfragrance ingredients are in actual use at any one time. Data from the FDA cosmetic voluntary reporting program indicate that approximately 700 of these 2300 ingredients have been reported to be used in 20 or more cosmetic formulations. The 700 ingredients whose reported frequency of use is greater than 20 are the ingredients that have thus far been prioritized for CIR review. Although we have prioritized only those cosmetic ingredients used in 20 or more formulations, in going through this process we have actually considered a much larger number of ingredients. We considered all ingredients in 10 or more formulations when we established the 1984 priority list, to make sure that important chemicals were not missed. And in 1987 FDA provided to the Expert Panel a list of all chemicals used in any cosmetic formulation, again to be sure that any important chemical was included. Thus, we have cast a wide net. One-third of these 700 ingredients are already regulated by FDA for use in food or drug products or as color additives.

## THE REVIEW PROCESS

### Scientific Literature Review

After an ingredient has been prioritized for review, the CIR staff prepares a scientific literature review which contains all of the available published safety information. This includes the cosmetic and noncosmetic uses, the physical and chemical characteristics of the ingredient, and any impurities that may be present. All safety data available to the staff are documented in accordance with an outline approved by the CIR Expert Panel for toxicology data presentation. The

CIR staff does not write or express any opinion on the validity or significance of the data. The CIR scientific literature review documents known data. The interpretation of data is done only by the CIR Expert Panel during its review of the ingredient. Where ingredients are chemically and toxicologically similar they may be grouped for review.

The Scientific Literature Review is then released for a 90-day public comment period with a request to industry and all other interested parties to provide any unpublished safety test data they may have in their files, as well as for any comments or suggestions to improve the report.

After the 90-day public comment period, the unpublished data submitted by industry and others are incorporated into the scientific literature review. Because much of the data is from unpublished reports, CIR is careful to document the actual available data, rather than to give brief summaries. The final Scientific Literature Review is then transmitted to the CIR Expert Panel for its evaluation.

After a review of all the information in the scientific literature review, the CIR Expert Panel makes its determination on safety. The CIR Procedures specifically require that the Panel make one of three decisions: safe for use, with or without limitations; unsafe for use; or insufficient data to make a determination on safety.

To accelerate the review, the CIR Expert Panel has divided itself into two working teams for the initial review and preparation of a report. Normally this takes two or three working sessions. After these review meetings, a draft report goes to the full CIR Expert Panel which evaluates the document in a series of public meetings.

If the ingredient is judged to be either safe or unsafe, a Tentative Final Report is released for a 90-day public comment period. After public comment is received, a Final Report is issued. If an insufficient data determination is reached, industry is notified. The specific type of safety test data required by the Expert Panel before a decision will be made is detailed. If no commitment to test is made, a Tentative Final Report stating that insufficient data are available is then released for the final 90-day comment period. When a manufacturer agrees to provide the additional test data requested in the Insufficient Data Announcement, the Expert Panel defers further review until the new test data are available. If that does not occur, a Final Report is issued determining that there are insufficient data.

The Expert Panel has expressed concern about the justification of additional animal testing. The Expert Panel has advised industry that "no new acute (LD50) test should be conducted on any ingredient under review for submittal to the Expert Panel unless specifically requested. The Panel will accept and include all existing LD50 data in its reports."

Any person may comment on these CIR documents, agreeing or disagreeing with them. The CIR Expert Panel must respond to every comment in the Final Report. All unpublished data cited in CIR Reports are publicly available to any interested person. At any meeting of the CIR Expert Panel, any interested individual may request to address the Panel on any ingredient under review by the Panel. The Expert Panel has always permitted any individual in attendance at its meetings to provide comments or ask questions on the topic or report under review. Thus, the program is open to full public scrutiny and must be responsive to all public comment.

After a Final Report is issued, it is submitted to the Journal of the American College of Toxicology for their editorial review prior to publication in a special edition of that Journal. These CIR reports are now being translated into Japanese and republished in Japan. Fourteen journal issues containing CIR Reports are now available. The fifteenth issue has already been reviewed and accepted for publication.

Upon request, CIR makes its reports and all unpublished data available to governmental health and regulatory agencies at no charge. In the United States, the CIR reports are routinely sent to the Food and Drug Administration, the National Institute for Environmental Health, the Consumer Product Safety Commission, and the National Cancer Institute. CIR has an active exchange program of reports and data for use in responding to the European Economic Commission (EEC).

## SAFETY TEST DATA NEEDED BY THE EXPERT PANEL

The data ordinarily considered adequate for a scientific evaluation by the CIR Expert Panel include:

1. A detailed chemical definition of the ingredient, including specifications and impurities.
2. The use of the ingredient in cosmetic products, including the concentration of use in each product category.
3. Animal safety test data, which may include subchronic and chronic toxicity, eye irritation, skin irritation and sensitization, and mutagenicity tests.
4. Human safety test data, which may include skin irritation, sensitivity, and photoallergenicity.

In determining the scientific test data needed to substantiate the safety of a cosmetic ingredient, the CIR Expert Panel applies generally accepted principles of toxicological evaluation. Rather than using an arbitrary list of standard tests, the Expert Panel determines the test data needed for an ingredient by reviewing all aspects of that particular substance.

In many instances, all data needed for an evaluation by the Expert Panel already exist. In some instances, further tests are required. Experience with the CIR review has shown that the careful and methodical scientific review given by the Expert Panel, and the documentation of the specific need for any additional testing requested by the Expert Panel, normally prompts the industry to do any testing required to prove safety. The full public discussion of the scientific rationale for requesting further testing, rather than a boilerplate "checklist" approach, places the burden of publicly defining the need to test on the Expert Panel.

Because the Expert Panel bases its evaluation on the characteristics, use, and all related factors pertaining to each individual ingredient, there is no set list of test data that are always required. The data used in evaluating any ingredient will depend upon all information available about that particular ingredient.

Should the data indicate a need for additional specific tests, such tests must be conducted. For example, the Expert Panel's concern about possible skin depigmentation caused by the ingredient p-hydroxyanisole prompted a request by the Expert Panel for a special study of the depigmentation potential of this ingredient. The testing was undertaken by a CTFA member. The Expert Panel's concern about the lack of a safe threshold exposure level ultimately prompted a decision by the Expert Panel that the ingredient was unsafe for use in cosmetic products under any conditions.

## PROGRAM RESULTS

As of August 1,1988, the Expert Panel has issued 112 Final Reports covering 277 ingredients. In the course of completing these reports, the Expert Panel issued 22 Insufficient Data Announcements. Thirteen of these announcements resulted in a response supplying the appropriate data required to make a decision on the safety of the ingredients, but nine did not. Of the 277 ingredients reviewed, the Expert Panel concluded that 237 are safe for use in cosmetics at the present practices of use (Table 1). Use limitations have been included in the conclusions of 18 reports for 30 ingredients (Table 2). For nine ingredients, reports have been released stating that there were insufficient data to judge safety. One report was released in which the Expert Panel found the ingredient, p-hydroxyanisole, unsafe for use in cosmetics (Table 3). There are currently 32 reports on 49 ingredients at various stages of development and review (Table 4).

## CURRENT CIR REVIEW STATUS OF INGREDIENTS

The current CIR status of the 700 most frequently used cosmetic ingredients is as follows:

| STATUS | | |
|---|---|---|
| Already reviewed by CIR | 39 percent | (277) |
| Under review by CIR | 9 percent | (49) |
| Scheduled for review by CIR | 15 percent | (111) |
| Deferred, awaiting FDA OTC Report | 19 percent | (133) |
| Exempt (RIFM ingredients) | 2 percent | (14) |
| Exempt (regulated by FDA) | 16 percent | (112) |

The time required to complete a report depends on the adequacy and amount of available safety test data. Normally it requires about 15-18 months to complete a report. Six of these 15 months are imposed procedural periods for the two 90-day public comment periods for the scientific literature review and the Tentative Final Report.

CIR continually monitors the status of all ingredients on its priority list. Of the 49 ingredients currently under review, 70 percent are already approved for use in Japan, and an additional 10 percent are safe for use in the United States for nonprescription drugs or as direct food additives. Twenty percent have no referenced food or drug use.

Similar data is available for the 111 ingredients on the priority list which are scheduled for CIR review. Forty-six percent are approved for use in Japan, and an additional 10 percent are safe for use in the United States in foods, and or, non-prescription drugs. Forty-four percent have no referenced United States approval for OTC drug or food use.

The European Economic Commission has not published a list of approved cosmetic ingredients. Only those that are prohibited or have restricted use conditions imposed are pblished on a list by the EEC. None of the prohibited ingredients are awaiting CIR review.

Summaries of the Expert Panel's conclusions in the 28 reports on ingredients which are unsafe under any conditions, have insufficient data, or are safe with limitations, as follows. The full reports on these ingredients present the discussion and rationale for each of these decisions.

## Unsafe Under Any Conditions

p-hydroxyanisole. The quality and quantity of available information was limited. Results of animal studies indicated that the ingredient was a skin sensitizer and a skin depigmenter. At a concentration of 2.0 percent, p-hydroxyanisole was not a human skin sensitizer. Clinical depigmentation data were inconclusive. This ingredient is not intended for use as a skin lightener or skin depigmenting agent in cosmetic products. Because of the depigmenting action of this ingredient in black guinea pigs at concentrations approaching those used in cosmetics, and because of *in vitro* toxicity to guinea pig melanocytes, the Expert Panel concluded that p-hydroxyanisole is unsafe for use as a cosmetic ingredient.

## Insufficient Data

benzyl paraben. There is a lack of safety test data on UV absorption, impurities, subchronic oral toxicity (subchronic feeding study), mutagenicity and/or in vitro genotoxicity, and eye irritation. If sufficient toxicity were shown in these studies, metabolism and associated pharmacokinetic studies may also be required. The CIR Expert Panel concluded that the available data were insufficient to support the safety of benzylparaben as used in cosmetics.

captan. Other than clinical studies, there were no dermal toxicity data on captan. Because captan is hydrolyzed in the gastrointestinal tract before it is absorbed, and because the toxicity of captan varies greatly with the route of administration, oral studies are not sufficient to determine the safety of captan as a cosmetic ingredient. Because captan is mutagenic in vitro, has produced intestinal neoplasms in mice following oral administration, and upon degradation becomes an electrophile, the Expert Panel concluded that it is necessary to require an 18-month skin carcinogenicity bioassay in mice. The CIR Expert Panel concluded that the available data were insufficient to support the safety of captan as used in cosmetics.

drometrizole. There is a lack of data on subchronic oral toxicity and on mutagenicity. Mutagenicity tests in two systems other than the Ames assay and the mouse bone marrow micronucleus test were requested. The Expert Panel concluded that the available safety data were insufficient to support the safety of drometrizole as used in cosmetics.

glyceryl ricinoleate. There is a lack of data on 28 day dermal toxicity in guinea pigs and on clinical sensitization and photosensitization potentials. The Expert Panel concluded that the available data were insufficient to support the safety of glyceryl ricinoleate as used in cosmetics.

morpholine. Morpholine reacts easily with N-nitrosating agents to form N-nitrosomorpholine. Under conditions of use it is unlikely that morpholine is totally free of carcinogenic nitrosamines. The Expert Panel could not conclude that morpholine is safe for use in cosmetic products until such a time as analytical in-use data or the appropriate risk assessment has been obtained and evaluated.

2,3-napthalenediol. The available information on 2,3-napthalenediol lacks dermal irritation and photosensitization data, as well as 90-day subchronic dermal studies and chemical description and impurity data. The Expert Panel concluded that the available data were insufficient to support the safety of 2,3-napthalenediol as used in cosmetics.

o-cymen-5-ol. There are a lack of test data on skin absorption, chronic oral toxicity, human skin sensitization, phototoxicity, photoallergenicity, and mutagenesis. The Expert Panel concluded that the available data were insufficient to judge the safety of use of o-cymen-5-ol in cosmetic products.

t-butyl alcohol. The available information on t-butyl alcohol lacked human sensitization data. The Expert Panel concluded that the available data were insufficient to support the safety of t-butyl alcohol as used in cosmetics.

t-butyl hydroquinone. There are a lack of test data on animal depigmentation, human and animal melanocyte toxicity, and photosensitization. The Expert Panel concluded that the available data were insufficient to support the safety of t-butyl hydroquinone as used in cosmetics. (Subsequent to the release of the Final Report on t-butyl hydroquinone, a CTFA member advised CIR that the requested testing would be undertaken. The Expert Panel has agreed to review the new data when they become available.)

## Safe With Limitations

benzalkonium chloride. Benzalkonium chloride is a skin and ocular irritant to animals at concentrations greater than 0.1 percent. The ingredient is also a human skin irritant at concentrations greater than 0.1 percent, and sensitization is possible in persons having damaged skin. The Expert Panel concluded that benzalkonium chloride, at concentrations up to 0.1 percent free active ingredient, is safe as a cosmetic ingredient under present conditions of use.

benzethonium chloride and methylbenzethonium chloride. Because of skin and ocular irritation above 5.0 percent, the Expert Panel conclusion is qualified for safe use at 0.5 percent in cosmetics applied to the skin and 0.02 percent is safe for cosmetics used in the eye area.

2-bromo-2-nitropropane-1,3-diol (BNPD). BNPD is a skin irritant at 1.0 percent and may interact with amines to form nitrosamines. The Expert Panel conclusion limits use to 0.1 percent. BNPD should not be used under circumstances in which it may interact with amines and amides.

cocamide DEA, lauramide DEA, linoleamide DEA, and oleamide DEA. The Expert Panel recognized the lack of of subchronic oral toxicity data on three of the ingredients of this group. The low subchronic oral toxicity of lauramide DEA and the low acute oral toxicities of all four ingredients, as well as the chemical and structural similarities between the ingredients, indicate that cocamide DEA, linoleamide DEA, and oleamide DEA are not significantly toxic after oral administration. The Expert Panel concluded that these ingredients are safe as cosmetic ingredients at currently used concentrations. These chemicals should not be used as ingredients in cosmetic products containing N-nitrosating agents.

diisopropanolamine, triisopropanolamine, isopropanolamine, and mixed isopropanolamines. The Expert Panel concluded that these ingredients are safe as cosmetic ingredients in present practices of use and concentration, but that they should not be used in products containing N-nitrosating agents.

formaldehyde. Due to skin sensitization in some individuals, the concentration in cosmetics should be as low as is practicable, not to exceed 0.2 percent. The Expert Panel could not conclude that formaldehyde is safe for use in aerosol products.

hydroquinone and pyrocatechol. Hydroquinone is a weak skin depigmenter at 1.0 percent. After prolonged exposure, it is a skin irritant and sensitizer in some individuals. Pyrocatechol has toxicological characteristics which are similar to those of hydroquinone. Hydroquinone is a mild ocular irritant at low concentrations, and pyrocatechol is a severe ocular irritant at high concentrations. The Expert Panel concluded that hydroquinone and pyrocatechol are safe for cosmetic use at concentrations of 1.0 percent and less in formulations intended for brief, discontinuous use followed by rinsing from the skin and hair.

methylene chloride. Methylene chloride is irritating to the skin of animals and is slightly irritating to the skin of humans. There were no data available on the sensitization potential of methylene chloride in products which are intended for prolonged contact with the skin. The ingredient is unlikely to be a photosensitizing agent. Of seven different laboratory studies, one chronic mouse study indicated that methylene chloride was a carcinogen. Pharmacokinetic and metabolism studies have established that the metabolism of methylene chloride in the mouse differs quantitatively from other species studied, and this difference in metabolism could account for the positive tumorigenic response in the mouse. Considering all of the data, and in particular the pharmacokinetic and metabolism data, the Expert Panel concluded that the data are insufficient to establish methylene chloride as a human carcinogen. Due to the lack of human skin irritation and sensitization data on cosmetic products containing methylene chloride, the Expert Panel concluded that methylene chloride is safe for use in cosmetic products designed for brief discontinuous use.

n-butyl alcohol. The Expert Panel concluded that n-butyl alcohol is safe in nail preparations in the present practices of use and concentration.

2-nitro-p-phenylenediamine and 4-nitro-o-phenylenediamine. For those persons not sensitized, the Expert Panel concluded that these two ingredients are safe as cosmetic ingredients.

p-phenylenediamine. This ingredient is a known sensitizer. For those persons not sensitized, the Expert Panel concluded that this ingredient is safe as a hair dye ingredient.

propyl gallate. Human studies show significant sensitization at concentrations exceeding 10 percent. The Expert Panel conclusion states this ingredient is safe in cosmetic products at concentrations not exceeding 1.0 percent.

shellac. The Expert Panel's conclusion is limited to refined wax-free bleached or cosmetic grade shellac. It was concluded that shellac is safe for use in cosmetic formulations at concentrations up to 6 percent.

sodium borate and boric acid. These two ingredients are safe at concentrations up to 5.0 percent. Because of the increased absorption by damaged skin as compared to intact skin, and available adverse animal test data, the Expert Panel recommended that cosmetic products containing free sodium borate or boric acid at 5.0 percent or below should not be used on infant skin or injured skin.

sodium lauryl sulfate and ammonium lauryl sulfate. Both ingredients have been shown to be irritants following prolonged exposure at concentrations of 2.0 percent and greater. Possible hair loss and comedone formation have been reported. The Expert Panel concluded that both ingredients are safe for discontinuous, brief use followed by thorough rinsing from the skin. For cosmetic products intended for prolonged contact with the skin, concentrations should not exceed 1.0 percent.

triethanolamine (TEA), diethanolamine (DEA), and monoethanolamine (MEA). The Expert Panel concluded that these ingredients are safe for brief, discontinuous use followed by thorough rinsing from the skin. MEA should be used only in rinse-off products. Because of the possible eye and skin irritation of TEA and DEA, products intended for prolonged contact should contain these ingredients at concentrations not exceeding 5.0 percent. TEA and DEA should not be used in products containing N-nitrosating agents.

TEA-lauryl sulfate. Due to skin irritation at high concentrations, the Expert Panel recommended limiting the use concentration to a maximum of 10.5 percent.

## SAFETY TESTING BY CTFA MEMBERS

The experience of the Expert Panel provides information on cosmetic testing practices by the industry. A CIR staff analysis of 52 Final Reports reviewed the source of test data used by the Expert Panel in reaching a decision that the cosmetic ingredient was safe. The source of clinical data for 52 Final Reports was as follows:

- All 52 reports had human skin irritation data. The data in 39 of these reports came only from unpublished industry reports. Thus, over 70 percent of these reports and their safety conclusions depended upon unpublished industry safety test data.

- The human sensitization data used in 40 of 51 reports that were judged safe were available only from unpublished industry studies. (One of the 52 reports was insufficient due to the lack of human test results.) Over 80 percent of the safety conclusions in the first 52 reports depended upon unpublished industry data for sensitization.

- Twenty-six of 28 reports had only unpublished industry data for human phototoxicity.

More of the animal test data used by CIR has been from published data sources than the human test data. Roughly 40 percent of all animal test data that was included in the 52 Final CIR Reports came from unpublished industry data.

CIR recently updated this information on the next 45 Final Reports published in the Journal of the American College of Toxicology. This review also included a special notation on whether the unpublished industry data was from pure ingredient tests or from formulation testing.

The results from the review of these 45 reports show similar trends. Over 75 percent of all human safety test data came from unpublished industry data, two-thirds of which was from formulation studies and one-third from pure ingredient testing. The number of unpublished animal safety test studies, as compared to published studies, used to substantiate the safety in these reports has also increased.

## ACCEPTANCE OF PANEL DECISIONS

The CIR Program is a voluntary self-regulation program. The CIR Expert Panel has no enforcement power, so it is difficult to determine the compliance of the cosmetic industry with the Expert Panel decisions. The reported frequency of use data on ingredients that were judged to be either insufficient or unsafe has fallen significantly. The following table is based upon the most recent data available from FDA for ingredients whose safety evaluation was completed prior to 1986.

## IMPACT OF CIR CONCLUSIONS ON REPORTED USE

| Ingredient | Type of Conclusion | Date of Conclusion | Change in Use (%) as of 1/1/88 |
|---|---|---|---|
| p-Hydroxyanisole | Unsafe | 3/85 | -97 |
| t-Butyl Hydroquinone | Insufficient | 7/85 | -93 |
| Drometrizole | Insufficient | 4/86 | -71 |
| Benzylparaben | Insufficient | 12/85 | -87 |
| o-Cymen-5-ol | Insufficient | 8/83 | -91 |

In evaluating these data, it is important to recognize that there is often a substantial lag between the time of an actual formulation change and submission of a report to FDA reflecting that change.

CIR is always open to new information. If this Committee has any information which indicates that a cosmetic ingredient should be added to the priority list, we would like to have that information. CIR will take this information, complete the necessary staff analysis, and present it to the Expert Panel for their consideration at the scheduled January 1989 meeting. The Expert Panel's decision and rationale for acceptance or rejection of a requested accelerated review, or the addition of new ingredients to the priority list, will be sent to this Committee by mid-January.

## TABLE 1

## Ingredients Safe for Use in Cosmetic Products at Present Practices of Use and Concentration

Acetylated lanolin
Acetylated lanolin alcohol
Almond meal
Aluminum distearate
Aluminum tristearate
4-amino-2-hydroxytoluene
m-Aminophenol
o-Aminophenol
p-Aminophenol
Ammonium laureth sulfate
Ammonium stearate
Amyl acetate
Avocado oil

Beeswax
Behenyl alcohol
Benzophenone 1
Benzophenone 2
Benzophenone 3
Benzophenone 4
Benzophenone 5
Benzophenone 6
Benzophenone 8
Benzophenone 9
Benzophenone 11
Butane
Butyl acetate
Butylated hydroxyanisole
Butylene glycol
Butylparaben
Butyl stearate

Calcium stearate
Candilla wax
Caprylic/capric triglyceride
Carbomer 910
Carbomer 934
Carbomer 934P
Carbomer 940
Carbomer 941
Carbomer 962
Carnauba wax
Cellulose gum
Ceresine
Cetearyl alcohol
Cetearyl octanoate
Cetyl alcohol
Cetyl lactate
Cetyl palmitate
Cetyl stearate
Chloroxylenol
Cholesterol
Coconut acid
Coconut oil
Coleth 24

## TABLE 1 - Continued

### Ingredients Safe for Use in Cosmetic Products at Present Practices of Use and Concentration

Decyl oleate
Dehydroacetic acid
Dibutyl phthalate
Diisopropyl adipate
Dimethicone copolyol
Dimethyl phthalate
Dioctyl adipate
Dipropylene glycol
Disperse black 9
DMDM hydantoin

Emulsifying wax
Ethoxydiglycol
Ethyl acetate
Ethylparaben

Glyceryl oleate
Glyceryl stearate
Glyceryl stearate SE
Glycol distearate
Glycol stearate
Glycol stearate SE

Hexylene glycol
Hydrogenated coconut acid
Hydrogenated coconut oil
Hydrogenated lanolin
Hydrolyzed collagen
Hydroxyethylcellulose
Hydroxylated lanolin
Hydroxypropylcellulose
Hydroxypropyl methylcellulose

Imidazolidinyl urea
Isoamyl acetate
Isobutane
Isobutyl stearate
Isocetyl stearate
Isodecyl oleate
Isopentane
Isopropyl lanolate
Isopropyl myristate
Isopropyl palmitate
Isopropyl stearate
Isostearic acid
Isostearyl alcohol
Isostearyl neopentanoate

Japan wax

Laneth 5
Laneth 9 acetate
Laneth 10 acetate

## TABLE 1 - Continued

## Ingredients Safe for Use in Cosmetic Products at Present Practices of Use and Concentration

Laneth 16
Laneth 25
Lanolin
Lanolin acid
Lanolin alcohol
Lanolin oil
Laureth 4
Laureth 23
Lauric acid
Lithium stearate

Magnesium stearate
Methylcellulose
Methylparaben
2-Methylresorcinol
Microcrystalline wax
Montan wax
Myristic acid
Myristyl alcohol
Myristyl lactate
Myristyl myristate
Myristyl stearate

1-Napthol
Nonoxynol-2
Nonoxynol-4
Nonoxynol-8
Nonoxynol-9
Nonoxynol-10
Nonoxynol-12
Nonoxynol-14
Nonoxynol-15
Nonoxynol-30
Nonoxynol-40
Nonoxynol-50

Octyl dodecanol
Octyl palmitate
Octyl stearate
Oleic acid
Oleyl alcohol
Ozokerite

Palmitic acid
Panthenol
Pantothenic acid
Paraffin
PEG 20 lanolin
PEG 27 lanolin
PEG 30 lanolin
PEG 40 lanolin
PEG 50 lanolin
PEG 60 lanolin
PEG 75 lanolin

## TABLE 1 - Continued

### Ingredients Safe for Use in Cosmetic Products at Present Practices of Use and Concentration

PEG 85 lanolin
PEG 2 stearate
PEG 6 stearate
PEG 8 stearate
PEG 12 stearate
PEG 20 stearate
PEG 32 stearate
PEG 40 stearate
PEG 50 stearate
PEG 100 stearate
PEG 150 stearate
Petroleum distillate
Phenyltrimethicone
Polyamino sugar condensate
Polybutene
Polysorbate 20
Polysorbate 21
Polysorbate 40
Polysorbate 60
Polysorbate 61
Polysorbate 65
Polysorbate 80
Polysorbate 81
Polysorbate 85
Potassium-coco-hydrolyzed animal protein
Potassium sorbate
Potassium stearate
Propane
Propylene carbonate
Propylene glycol stearate
Propylene glycol stearate SE
Propylparaben
Polyquaternium-10

Quaternium-15
Quaternium-18
Quaternium-18 bentonite
Quaternium-18 hectorite

Resorcinol
Retinol
Retinyl palmitate

Safflower oil
Sodium bicarbonate
Sodium carbonate
Sodium dehydroacetate
Sodium laureth sulfate
Sodium lauryl sulfoacetate
Sodium sesquicarbonate
Sodium stearate
Sorbic acid
Sorbitan laurate
Sorbitan oleate
Sorbitan palmitate
Sorbitan sesquioleate

## TABLE 1 - Continued

## Ingredients Safe for Use in Cosmetic Products at Present Practices of Use and Concentration

Sorbitan stearate
Sorbitan trioleate
Sorbitan tristearate
Squalane
Squalene
Stearalkonium chloride
Steareth-2
Steareth-4
Steareth-6
Steareth-7
Steareth-10
Steareth-11
Steareth-13
Steareth-15
Steareth-20
Stearic Acid
Stearyl alcohol
Sweet almond oil
Synthetic beeswax
Synthetic wax

Tall oil
TEA-Coco-Hydrolyzed animal protein
Toluene
Toluenesulfonamide/formaldehyde resin
Toluenesulfonamide/formaldehyde resin - 80%
Tragacanth gum

Vinyl acetate/crotonic acid copolymer

Wheat flour
Wheat germ glycerides
Wheat germ oil
Wheat gluten
Wheat starch

Zinc phenolsulfonate
Zinc stearate

## TABLE 2

## Ingredients Which are Safe for Use in Cosmetics With Limitations

Ammonium lauryl sulfate

Benzalkonium chloride
Benzethonium chloride
Boric acid
2-Bromo-2-nitropropane-1,3-diol (BNPD)

Cocamide DEA

Diethanolamine (DEA)
Diisopropanolamine

Formaldehyde

Hydroquinone

Isopropanolamine

Lauramide DEA
Linoleamide DEA

Methylbenzethonium chloride
Methylene chloride
Mixed isopropanolamines
Monoethanolamine

n-Butyl alcohol
4-Nitro-o-phenylenediamine
2-Nitro-p-phenylenediamine

Oleamide DEA

p-Phenylenediamine
Propyl gallate
Pyrocatechol

Shellac
Sodium borate
Sodium lauryl sulfate

TEA-lauryl sulfate
Triethanolamine (TEA)
Triisopropanolamine

## Table 3

## Ingredients Which Had Insufficient Data or Which Were Unsafe

### Insufficient Data

Benzylparaben

Captan

Drometrizole

Glyceryl ricinoleate

Morpholine

2,3-Napthalenediol

o-Cymen-5-ol

t-Butyl alcohol

t-Butyl hydroquinone

### Unsafe for Cosmetic Use

p-Hydroxyanisole

## TABLE 4

## Ingredients Which are Currently Under Review

Aminomethylpropanediol
Aminomethylpropanol
Ammonium thioglycolate
Arachidyl propionate

5-Bromo-5-nitro-1,3-dioxane
Butyl myristate

Chloroacetamide
Cocamidopropyl betaine
Cocoamphoacetate
Cocoamphodiacetate
Cocoamphodipropionate
Cocoamphopropionate
Cyclomethicone

2,4-Diaminophenoxyethanol hydrochloride
Diazolidinyl urea
Dilauryl thiodipropionate
Disperse violet 1

Glutaral
Glyceryl thioglycolate

Hydrogenated tallow glyceride
Hydrogenated tallow glycerides
Hydroxybenzomorpholine

Isopropyl isostearate
Isopropyl linoleate

Jojoba oil

Lapyrium chloride

Methylchloroisothiazolinone
2-Methyl-5-hydroxyethylaminophenol
Methylisothiazolinone

1-Nonoxynol

Phenethyl alcohol
Phenoxyethanol
p-Methylaminophenol sulfate
Polyacrylamide
Potassium bromate
PPG-12-buteth-16
Pyrogallol

Sesame oil
Sodium bromate
Sodium cetearyl sulfate
Sodium dodecylbenzene sulfonate
Sodium myreth sulfate
Steapyrium chloride
Stearic hydrazide

Tallow
Tallow glyceride
Tallow glycerides
TEA-dodecylbenzenesulfonate
Thioglycolic acid

C·T·F·A
*The Cosmetic, Toiletry and Fragrance Association*

*E. Edward Kavanaugh*
*President*

STATEMENT OF

E. EDWARD KAVANAUGH

PRESIDENT

THE COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION, INC.

BEFORE

THE SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

OF

THE COMMITTEE ON SMALL BUSINESS

U.S. HOUSE OF REPRESENTATIVES

September 15, 1988

*1110 Vermont Avenue, NW • Suite 800 • Washington, DC 20005 • (202) 331-1770 • Telex 89-2673*

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# STATEMENT OF
# E. EDWARD KAVANAUGH
# PRESIDENT
# THE COSMETIC, TOILETRY AND FRAGRANCE ASSOCIATION, INC.
# BEFORE
# THE SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES
# OF
# THE COMMITTEE ON SMALL BUSINESS
# U.S. HOUSE OF REPRESENTATIVES

September 15, 1988

## INTRODUCTION

Mr. Chairman and members of the Subcommittee, I am Edward Kavanaugh, President of the Cosmetic, Toiletry and Fragrance Association (CTFA). Accompanying me are Mr. Frank Romano, a member of the Board of Directors of CTFA and Chairman and CEO of Key West Fragrance and Cosmetic Factory; Dr. G.N. McEwen, Jr., CTFA Vice President of Science; and Mr. Peter Barton Hutt, CTFA outside counsel and a partner in Covington and Burling.

CTFA is the national trade association representing the cosmetic, toiletry, and fragrance industry. Founded in 1894, CTFA has an active membership of more than 240 companies, which manufacture or distribute the vast majority of the finished cosmetic products marketed in the United

States. CTFA also includes more than 230 associate member companies, which sell services, equipment, or supplies, such as raw materials and packaging components, to active members. CTFA represents companies of all sizes. The annual sales of our individual members range from less than $500,000 to more than $3 billion. More than half of our members are small businesses with annual sales of less than $1 million.

CTFA is here today to discuss the safety of cosmetic products. We will make three major points:

1. Cosmetic products are among the safest consumer products available.

2. The cosmetic industry takes its responsibility to consumers seriously and has voluntarily initiated many programs to ensure the safety of its products.

3. The Food and Drug Administration (FDA) has -- and exercises -- abundant legal authority to regulate cosmetics.

## THE COSMETIC INDUSTRY

CTFA members are committed to providing consumers with a wide choice of safe, high quality cosmetic products. Everyone uses cosmetics. Chances are excellent that every person in this hearing room has used at least one cosmetic product within the last few hours. Toothpaste, mouthwash, shampoo, deodorant, shaving cream, shaving lotion, hair spray, cologne, suntan products, lipstick, mascara -- the list goes on and on. They are all cosmetics.

Cosmetics are manufactured and distributed by very small businesses as well as by very large ones. Together, these large and small cosmetic companies form a $17 billion industry that helps provide the livelihood for tens of thousands of Americans.

Cosmetic products are marketed through virtually every form of retail channel. They are sold by a wide variety of retail stores, by cosmetology salons, by neighborhood salespeople, and by direct mail.

The cosmetic industry has a long history. There is evidence of cosmetic use in every recorded civilization. For thousands of years, men and women have created cosmetic products from available raw materials to satisfy their fundamental human need for personal hygiene, self-assurance, and self-esteem. Modern industry has improved upon these traditional products by making them purer, safer, and more attractive than ever before.

## COSMETIC BENEFITS

That cosmetic products have been around for so long is one indication of their value. Medical authorities throughout the world agree that the enhanced appearance and psychological well-being that cosmetic products help provide is beneficial to consumers. Cosmetics do make a difference in how others see and respond to us and in how we feel about ourselves.

- In the words of Dr. Frank Young, Commissioner of FDA, "Cosmetics have played an increasingly important role in our individual lives. They allow people to feel better about themselves and change an aspect of their lives in a meaningful way."[1]

- According to Dr. Thomas Cash, Professor of Psychology at Virginia's Old Dominion University and one of the foremost authorities on the

> psychological effects of appearance, "Far from a frivolous luxury, cosmetics and grooming products are psychologically significant tools for the control, management, and enhancement of self-image and social image."[2]

## COSMETIC INDUSTRY SAFETY RECORD

### Introduction

The overwhelming evidence shows that cosmetic products have an exemplary and enviable safety record. In fact, cosmetics are among the safest consumer products available in the marketplace today.

As noted by FDA,

> "Safety measures developed by manufacturers, in cooperation with the FDA, have achieved a high degree of safety in cosmetic and toiletry products."[3]

At the same time, we must recognize that nothing in life is completely without risk. There is no way one can guarantee or prove complete safety under all circumstances. Cosmetics

-- like food, drugs, and all other consumer products -- occasionally do produce adverse reactions and injuries. Some of these represent the irreducible minimum of idiosyncratic reactions. Others are accidental or caused by the failure of the user to follow the manufacturer's directions for safe use. Still others result from the intentional misuse of a product for a purpose for which it was never intended.

Adverse reactions and injuries associated with cosmetic products are in most cases mild and temporary. They are also very few -- both in total number and in proportion to product use.

## North American Contact Dermatitis Group Study

A study of patients with skin problems, which was conducted by the North American Contact Dermatitis Group, offers evidence of the high degree of safety of cosmetic products. A report on this study published in the Journal of the American Academy of Dermatology states, "From an estimated 281,100 patients seen during the 64-month period and from the 13,216 contact dermatitis cases observed, 713 patients with cosmetic-related reactions were identified, representing 0.3 percent of the total patient population and

5.4 percent of all patients with contact dermatitis."[4] A December 1984 American Academy of Dermatology news release on this study concluded, "Makeup and other forms of beauty care preparations cause fewer allergic skin reactions than most people realize."[5]

## Voluntary Reporting Program Data

The data collected under the FDA Voluntary Cosmetic Reporting Program provide further evidence that cosmetics are safe. Under one part of that program, cosmetic companies submit to FDA information on adverse product reactions. Averaged for the period 1983-1986, these data indicate there were approximately 1.6 reported reactions for every million products distributed.[6] Since most cosmetic products are used more than once, there would actually be even fewer reactions per product use, a more direct comparison. Moreover, most of the reported incidents involved minor and temporary reactions.

## NEISS Data

Properly interpreted, data from the Consumer Product Safety Commission's National Electronic Injury Surveillance System

(NEISS) support the excellent safety record of cosmetics.

NEISS collects reports on "injuries" related to various categories of consumer products, including cosmetics, from a sample of hospital emergency rooms. On the basis of 761 cosmetic-related incidents treated in the 62 NEISS sample emergency rooms in 1987, it was estimated at a July 14, 1988, hearing before this Subcommittee that approximately 47,000 cosmetic "induced" injuries occurred nationwide during that year.

We asked a statistician to examine the NEISS data relating to cosmetic products. His report,[7] which we will submit for the record, explains that the NEISS data have been widely and properly criticized by the Consumer Product Safety Commission itself as well as outside experts for failing to meet important criteria of statistical soundness and usefulness. In fact, the deficiencies are such that the FDA and the Center for Disease Control have reportedly stopped using NEISS data.[8]

Putting aside the underlying concerns about the general quality of the data base, however, the report shows two important things.

- The estimate of 47,000 was derived through an unsound analysis of the data and is much too high.

- The vast majority of the injuries that did occur were not severe.

The statistician's analysis of the NEISS data that meet CPSC's own criteria for reliability and that appear on the basis of the descriptions available to have been caused by a cosmetic product rather than by product misuse or carelessness, suggests that one might project approximately 20,000 incidents, not 47,000, for 1987. Since about 9 billion cosmetic products are sold annually, we can use that better projection and the NEISS data to hypothesize that there were fewer than 2.5 incidents for every million products sold.

To carry the discussion a step further, consider once again the fact that each product sold generally represents many product use experiences. With a conservative estimate that products are used an average of only ten times each, one can hypothesize that there were 0.2 incidents for every million uses.

Even if one were to accept the estimate of 47,000 cosmetic "induced" injuries, which, as we have explained, we do not, it can be put in perspective by comparing it to NEISS estimates for some other common consumer products during the same period. For example, according to the most recent NEISS Product Summary Report[9] there were:

- 71,572 incidents related to sofas and couches;
- 77,384 incidents related to metal containers;
- 117,696 incidents related to drinking glasses; and
- 253,538 incidents related to various types of beds, mattresses, and pillows.

It would appear that the Congress should be looking into the regulation of beds and pillows rather than cosmetics.

The statistician's report makes two important points that are essential to a clear understanding of the projected cosmetic-related incidents:.

- First, the NEISS data reflect incidents related to, but not necessarily caused by, consumer products.

- Second, some of the incidents reported by NEISS did not result in any real injury.

Let us illustrate both of these points.

NEISS literature clearly warns that the data "are based on injuries treated in hospital emergency rooms that patients say are related to products. Therefore it is incorrect, when using NEISS data, to say the injuries were caused by the product."[10]

The injuries reflected by the NEISS data, to use its own terminology, were related to the various products. They were not necessarily caused by them. To illustrate, a NEISS computer printout[11] that briefly describes the circumstances surrounding the sample of 761 actual incidents on which the projection of the 47,000 alleged cosmetic-related injuries is based, includes the following:

- "A perfume bottle fell off shelf and struck his face."

- "Lacerated left thumb while carving soap with sharp knife . . . "

- "While in shower, [patient] bent over to pick up soap and developed severe back pain."

- "Attempted overdose of isopropyl alcohol and hair tonic."
- "He went to reach for shampoo, glass soap dish fell on foot, cutting foot . . ."
- "Put baby powder with water in eyes for cleaning purposes . . ."
- "Broke a bottle with bathsalts in it."
- "Hit self in eye while removing eye-makeup."

The resulting injuries, regrettable as they are, were either not caused by the cosmetic product or were caused by misuse of the product.

Furthermore, some events reported as "injuries" under the NEISS system are not in fact injuries. For example, if a child were to swallow a bite of lipstick and be rushed to the emergency room by a panic-stricken parent, the incident would be reported as an "injury" even though the child was not really injured in any way.

The NEISS printout is replete with examples of similar incidents, which were related to a cosmetic but were clearly not caused by the product itself or which did not in fact result in any real injury. The inclusion of these kinds of incidents in the NEISS data makes it impossible to use the data without evaluation as an accurate measure of the number of real injuries caused by cosmetic products.

The NEISS data do indicate that the vast majority of the cosmetic-related injuries were not severe. Less than 1 percent of such injuries occurring during 1987 were severe enough to warrant hospitalization.

## Jeri-curl Products

There are, of course, exceptions to the rule that adverse reactions involving cosmetics are generally mild and transient. There was testimony at the July hearing regarding a tragic incident involving a woman whose hair caught on fire after she used an ethnic hair care product referred to as a "jeri-curl" product. It was a terrible accident. No doubt this woman has suffered greatly.

The accident in question was apparently caused by something the manufacturer did not foresee -- the head of a match broke off, went into her hair, and set it on fire. We don't know to what extent the jeri-curl product did or did not contribute to the fire once it was started.

We simply do not know enough about this particular product to say whether it poses an unacceptable hazard. This accident was awful, but thousands of other consumers have used the same and similar products time and time again without injury. If this product does have unacceptable flammability characteristics, the FDA has authority to take regulatory action.

## INDUSTRY SAFETY PROGRAMS

### Introduction

We deplore any adverse reactions. Even one injury is one too many. We will not relax our long and successful efforts on behalf of consumer safety. The welfare of millions of consumers depends on the safety of our products. That is a grave responsibility, and we take it very seriously.

To help cosmetic manufacturers meet that responsibility, the industry supports a number of effective and highly-respected voluntary programs, which help ensure product safety by providing information to cosmetic manufacturers, FDA, and the public.

The Cosmetic Ingredient Review Program and Procedures

The cornerstone of the industry's efforts to ensure the safety of its products is the Cosmetic Ingredient Review (CIR) program. This industry-funded program was established 12 years ago to help manufacturers meet their moral and legal obligation to ensure that each ingredient used in a cosmetic and each finished cosmetic product is safe before it is marketed. Dr. Robert Elder, Director of CIR, has described the program and its procedures in detail in his testimony. We would like simply to reiterate a few points.

CIR brings together all available scientific data on the safety of cosmetic ingredients for review and further evaluation by an independent Expert Panel of seven leading academic scientists and physicians. CIR procedures, which mirror and in fact were patterned after FDA procedures for the Over-the-counter (OTC) Drug Review and Biologics Review, ensure the Expert Panel complete independence to assess the data on these ingredients.

Priorities for CIR review of ingredients are set by a formula that takes into account eight factors relating to each ingredient. These factors include such things as information on biologic effects, which is found in the scientific literature, and information on the frequency of use of ingredients in cosmetics, which is obtained from data generated by FDA in connection with the FDA Voluntary Cosmetic Reporting Program. The Expert Panel has the final say on the priority list and may change it at any time.

Once priorities are assigned, the next step in the review process is the compilation by CIR's technical support staff of a scientific literature review that summarizes all available published and unpublished data on the ingredient under review. The data, which are collected from around the world, include a variety of human, animal, and *in vitro* studies that relate to the individual ingredient and to finished products that contain it.

The Expert Panel reviews and evaluates the collected data. It determines that the ingredient is safe for use in cosmetics with or without limitations; that the ingredient is unsafe for such use; or that there are insufficient data to determine whether the ingredient is safe or unsafe.

The Expert Panel then publishes a report of its findings, which is made available to FDA and the public as well as to the industry. The Expert Panel's decisions and opinions are publicly announced without any prior approval by the cosmetic industry.

Policy direction for CIR comes from a Steering Committee, which includes two academic appointees selected by the American Academy of Dermatology and the Society of Toxicology; the Chairman of CTFA's Scientific Advisory Committee; and CTFA's President and Vice President--Science. The Steering Committee does not participate in the scientific evaluations conducted by the Expert Panel.

The seven distinguished members of the CIR Expert Panel were selected by the Steering Committee from a group of academic scientists and clinicians nominated by consumer organizations, scientific and clinical societies, and government agencies. They represent the disciplines of dermatology, pharmacology, chemistry, toxicology, and oncology.

All Expert Panel members must meet conflict-of-interest standards that are the same as those applied under federal law to special government employees, such as FDA advisory committee members. Before being appointed to the Expert Panel, nominees are screened to determine that they have no financial relationship with any cosmetic-related company whose products or ingredients could be subject to Expert Panel review. This includes such areas as employment by the industry, research grants or contracts, and stock and bond holdings.

The Expert Panel has three liaison representatives or contact persons. FDA, the Consumer Federation of America, and CTFA each appoint one of these nonvoting representatives.

CIR is widely recognized as better, faster, and more cost effective than most other review programs -- including FDA's own OTC Drug Review. The CIR program has been commended by FDA, consumer groups, and the scientific community. For example:

- FDA Commissioner Frank Young has called CIR "an authoritative national and international voice on cosmetic ingredient safety." According to Dr. Young, "Such an accomplishment is only possible when an industry is fully committed to a program of this stature, and the participants consistently base their decisions on sound science, good judgment, and the highest levels of integrity."[12]

- The current Consumer Federation of America liaison representative to CIR has stated, "Having seen the panel in action, I must say that I am impressed extremely by both the caliber and interest of the panel members and by the extensive productivity of the group."[13]

CIR's Contribution to Product Safety

The sole purpose of CIR is to determine the safety of cosmetic ingredients. Ingredients, such as color additives, that are directly regulated by FDA are excluded. Those subject to other reviews by FDA (e.g., food and drug substances) or industry (e.g., fragrances) are deferred. All the rest are prioritized and reviewed by CIR.

In the next three to five years, CIR will have reviewed the safety of the chemicals used in 20 or more cosmetic formulations. Of the 277 ingredients reviewed so far, 237 were determined to be safe as used, 30 were found to be safe with specific limitations on concentration or on the types of formulations in which they can be used safely, nine were found to have insufficient data, and one was judged to be unsafe for use in cosmetics because it would bleach the skin, which is a drug action.

Each CIR report determining that an ingredient is safe represents a scientific judgment that sufficient testing has been done on the ingredient and that more testing is not needed. Where the Expert Panel determines that testing is warranted for an ingredient but has not been done, it does not find that ingredient safe for use in cosmetic products until the appropriate testing has been done and reviewed.

As of January 1, 1988, CIR had released 101 final reports, some of which covered more than one ingredient. Seventy percent of those reports contain long-term carcinogenicity or mutagenicity test data that have been judged to be sufficient to make a determination that the ingredients do not have a potential to cause chronic toxic effects in products. For each report that does not contain such data, the Expert Panel has fully evaluated the compounds and has determined that no such data are necessary.

FDA uses a similar approach to determine whether carcinogenicity or mutagenicity studies are required in support of a food or color additive petition. To make such determinations, the agency has developed and applies a comprehensive set of criteria based on existing scientific knowledge about structure/activity relationships and other factors.[14] Thus, the CIR Expert Panel uses the same type of toxicologic judgment as FDA in making these decisions.

CIR is supplemented by a companion program operated by the Research Institute for Fragrance Materials (RIFM), which reviews the safety of fragrance ingredients. The CIR and RIFM programs are very effective. Use of p-Hydroxyanisole, for example, was eliminated following CIR's finding that it is unsafe for cosmetic use. Uses of AETT and 6-methyl coumarin, two fragrance ingredients judged unsafe by RIFM, have also been eliminated by the cosmetic industry. These voluntary industry actions made it unnecessary for FDA to take regulatory action in connection with these chemicals.

According to former FDA Commissioner Arthur Hull Hayes, Jr.,

> "Both [the CIR and RIFM] programs are remarkable and noble efforts. More than anything, they demonstrate your resolve to review the safety of the raw materials your industry uses, to carry out testing where gaps of knowledge exist and to weed out those materials that may harm consumers when used in your products as ingredients.
>
> "The wealth of information assembled here has also been, and will continue to be, enormously helpful to us at FDA in performing our task. But most importantly, these programs are helping consumers. They are reducing toxicological uncertainties at the same time they allow consumers to place greater trust in the safety of your products."[15]

Some of the beneficial and useful cosmetic and fragrance ingredients that at times come under attack by the scientifically uninformed have in fact been reviewed and found safe under conditions of use by CIR or some other authoritative body. One example is formaldehyde. The CIR Expert Panel's report found that "formaldehyde in cosmetic products is safe to the great majority of consumers. The Panel believes that because of skin sensitivity of some individuals to this agent, the formulation and manufacture of a cosmetic product should be such as to ensure use at the minimal effective concentration of formaldehyde, not to exceed 0.2 percent measured as free formaldehyde. . . ."[16]

This finding was confirmed by FDA, which evaluated formaldehyde inhalation studies on laboratory animals and concluded that the potential exposure from FDA-regulated products was so insignificant that it did not warrant regulatory action. In a March 12, 1986, letter to the International President of the United Food and Commercial Workers Union (UFCW), Dr. Sanford Miller, then Director of FDA's Center for Food Safety and Applied Nutrition, stated, "We have also learned . . . that the use of formaldehyde as a preservative in shampoos and other cosmetic products does not present a carcinogenic risk, that its risk of causing allergic reactions is minimal, and that its usefulness by preventing microbial contamination and potential blindness far outweighs any toxic consideration."[17]

## The Voluntary Cosmetic Reporting Program

The Voluntary Cosmetic Reporting Program, which has been in operation since the early 1970's, is an important element of the industry's self-regulation efforts. Under this program, many cosmetic companies voluntarily register their plants and provide FDA with information on formulations and with product adverse reactions. Procedures relating to voluntary program participation are established by FDA regulations.[18]

The information provided under the Voluntary Cosmetic Reporting Program helps the government protect public health. FDA uses it for trend analyses as well as other purposes. For example, the agency relied on Voluntary Cosmetic Reporting Program adverse reaction data to support the need for a regulation mandating warning labels on bubble bath products.[19] The data are also helpful to the industry's CIR program, which uses FDA statistical compilations as one element in determining priorities for reviewing the safety of cosmetic ingredients.

Referring to data collected under the Voluntary Reporting Program, former FDA Commissioner Arthur Hull Hayes, Jr., said, "This body of information has been enormously helpful to us in our regulatory and enforcement efforts. Your voluntary registrations have enabled us to expand our inspectional efforts and have on several occasions aided us greatly in identifying products containing ingredients that were found to be hazardous to consumers under conditions of product use."[20]

The companies participating in the Voluntary Reporting Program are responsible for the vast majority of the cosmetic products sold in the United States. We are encouraged by this, but we are also committed to increasing the level of participation.

We recognize that voluntary programs are never 100 percent effective, but neither are programs mandated by law or government regulation. For example, an FDA survey of compliance with a regulation requiring pharmacies to distribute patient package inserts for estrogens found that the inserts were dispensed spontaneously, as mandated, in only 39 percent of the pharmacies surveyed.[21] Similarly, how many stores still post the required saccharin warning notices?

## Technical Publications

CTFA's development and dissemination of information to help manufacturers identify cosmetic ingredients, maintain the integrity of the manufacturing process, and provide consumers with meaningful information on their products, also play vital roles in the industry's safety program. For example,

- The _CTFA Technical Guidelines_ are invaluable in the establishment and maintenance of up-to-date quality and safety assurance programs. They address how to develop programs to ensure preservative efficacy and manufacturing quality control, and how to develop safety substantiation programs.

  We support cosmetic good manufacturing practices. In July 1977, in fact, CTFA petitioned the FDA to adopt good manufacturing practices regulations for cosmetic products. The agency never acted on our petition. Former FDA Commissioner Arthur Hull Hayes, Jr., credited the _Guidelines_ with having made the promulgation of such regulations unnecessary.[22]

  According to FDA Commissioner Young, "With limited government resources, self-regulation through CTFA's _Technical Guidelines_ is essential for safe, uncontaminated products."[23]

- The CTFA Compendium of Cosmetic Ingredient Composition provides comprehensive and authoritative information on raw materials used in cosmetics. It includes specifications that chemically characterize and define desirable quality criteria for cosmetic ingredients. Although the specifications are strictly voluntary, many cosmetic companies use them as published. Others use them as a starting point for development of their own internal standards to help assure consumer safety and the quality of their products.

- The CTFA Cosmetic Ingredient Dictionary and Supplement provide the industry, the medical profession, the government, and consumers with a specific chemical definition and ingredient nomenclature for cosmetic ingredients. Developed voluntarily by CTFA and the cosmetic industry, the Dictionary is recognized by FDA regulations as a source for proper ingredient nomenclature for the purposes of cosmetic ingredient labeling.[24]

- CTFA's Scientific Monograph Series is a group of papers by leading scientists on subjects of importance to the industry.

- Another CTFA publication, Microtopics, provides a collection of paper presentations, reports of test studies, and articles to help achieve a better understanding of product preservation adequacy and testing.

- CTFA's Labeling Manual outlines FDA and other federal agency labeling rules and offers an analysis of each regulation to help companies of all sizes understand and comply with these often complex requirements.

- Cosmetic Industry on Call is another of the industry's public-service publications. When a cosmetic product is associated with an adverse reaction, the cosmetic industry cooperates fully with the medical profession to evaluate the problem. To facilitate such efforts, CTFA works with the American Academy of Dermatology (AAD) to distribute to dermatologists copies of Cosmetic Industry on Call, a directory of the names, addresses, and telephone numbers of cosmetic company employees responsible for responding to requests for information on cosmetic ingredients and formulations. CTFA just printed a new edition of this publication in August 1988 and has provided sufficient copies for distribution to all AAD members and to other groups.

## Conclusion

The industry has instituted a number of programs that are sound examples of effective, voluntary self regulation. They conserve government and industry resources while, at the same time, help ensure the availability of safe, high quality products for American consumers.

Several FDA Commissioners have had high praise for the cosmetic industry's voluntary programs. For example:

> According to Commissioner Frank Young, "Voluntary efforts toward safe products have been the hallmark of [the cosmetic] industry."[25]

> According to former Commissioner Arthur Hull Hayes, Jr., the cosmetic industry "may be viewed as a striking example of what can be accomplished in the spirit of voluntarism. There has been no epidemic of serious adverse reactions to cosmetics and, in spite of the impressive advances in science and

> technology, as well as in consumer awareness, Congress has repeatedly seen no reason to amend the cosmetic provisions of the FD&C Act as it has with respect to food and color additives, drugs and medical devices."[26]

> Former Commissioner Alexander Schmidt said, "I can honestly say that I know of no industry which has a better record of voluntary accomplishment."[27]

## FDA AUTHORITY TO REGULATE COSMETICS

### Introduction

FDA has abundant legal authority under the Federal Food, Drug, and Cosmetic Act (FD&C Act)[28] to ensure that the cosmetic industry lives up to its voluntary commitment to safe products. The agency, however, has had relatively little need to exercise that authority because cosmetics are generally composed of relatively innocuous ingredients. Unlike drugs, which have ingredients intended to exert a pharmacologic effect, cosmetic ingredients are largely inert and thus pose no significant risk. When necessary, the industry has also acted voluntarily to prevent safety problems. Under these circumstances, the absence of extensive regulatory action is a tribute to the cosmetic industry. It should not be turned into an argument for broader government regulation. Broader regulation is not needed and would only waste industry, government, and public resources.

## The Federal Food, Drug, and Cosmetic Act

The FD&C Act clearly requires cosmetic manufacturers to ensure that their products are safe.

- Section 301(a)[29] prohibits "the introduction or delivery for introduction into interstate commerce of any . . . cosmetic that is adulterated or misbranded."

- Section 601[30] describes circumstances under which a cosmetic will be deemed "adulterated." These are

  a. If it bears or contains a poisonous or deleterious substance that may make it injurious under the conditions of use prescribed in its labeling or under customary or usual conditions of use. The law provides a single exception for coal-tar hair dyes that bear prescribed warning statements.

b. If it consists of any filthy, putrid, or decomposed substance.

c. If it was prepared, packed, or held under unsanitary conditions whereby it may have become contaminated with filth or rendered injurious to health.

d. If its container is made of a poisonous or deleterious substance that may make the contents injurious to health.

e. If it is not a hair dye and is, bears, or contains a color additive that is unsafe under section 706(a) of the FD&C Act.

- Section 706[31] requires FDA to approve color additives for safe use before they can be used in cosmetics and specifically prohibits the agency from balancing benefits against risks in its evaluation of color additive safety.

- Section 602[32] describes when a product will be deemed "misbranded." These circumstances include:

  a. If its labeling is false or misleading in any particular.

  b. If it is in package form and not labeled with the name and place of business of its manufacturer, packer, or distributor and with an accurate statement of quantity.

  c. If any word, statement, or other information required by law or regulation to appear on the label is not prominently on the label with such conspicuousness and in such terms that make it likely to be read and understood by an ordinary individual under customary conditions of purchase and use.

  d. If its container is so made or filled as to be misleading.

  e. If it is a color additive and its packaging and labeling do not conform with applicable requirements.

f. If its packaging or labeling violates an applicable regulation issued under the Poison Prevention Packaging Act.

- Section 201(n)[33] provides that in determining whether a cosmetic is misbranded because of misleading labeling, one must take into account, among other things, not only the representations made or suggested by statement, word, design, device, or any combination thereof, but also the extent to which the labeling fails to reveal facts that are material in the light of the representations or with respect to the consequences that may result from use under the conditions prescribed in the labeling or under customary or usual conditions of use.

FDA has adequate authority to regulate cosmetic products under the provisions of the FD&C Act. It can ban or restrict ingredients for safety reasons, mandate warning labels, inspect manufacturing facilities, issue regulatory letters, seize illegal products, enjoin unlawful activities, prosecute violators, and engage in nationwide recalls. The agency's formidable enforcement powers ensure that the cosmetic industry maintains safe products.

FDA's Safety Substantiation Regulation

FDA has in fact promulgated numerous regulations to implement these statutory provisions relating to cosmetic safety. The keystone of these regulations requires that the safety of each ingredient and of the finished cosmetic product be adequately substantiated before marketing:

> "Each ingredient used in a cosmetic product and each finished cosmetic product shall be adequately substantiated for safety prior to marketing. Any such ingredient or product whose safety is not adequately substantiated prior to marketing is misbranded unless it contains the following conspicuous statement on the principal display panel: Warning--The safety of this product has not been determined."[34]

The preamble published in the Federal Register when this regulation was adopted in 1975 provides some guidance from FDA concerning what constitutes adequate safety substantiation. It states that:

> " . . . the safety of a product can be adequately substantiated through (a) reliance on already available toxicological test data on individual

> ingredients and on product formulations that are similar in composition to the particular cosmetic, and (b) performance of any additional toxicological and other tests that are appropriate in the light of such existing data and information. . . . The Commissioner recognizes that there often is scientific controversy concerning the amount of data necessary to demonstrate the safety of a cosmetic. It is not the intention of the regulation to require the warning statement in circumstances where reasonable scientific opinion would regard the available data as adequate."[35]

CIR helps cosmetic manufacturers comply with the FDA's safety substantiation requirements. CIR's function is to review and evaluate data on the safety of cosmetic ingredients. During the course of each review the Expert Panel does consider available testing data on finished products that contain the ingredient under review. It is the responsibility of each cosmetic manufacturer, however, to substantiate the safety of its finished cosmetic products.

In substantiating the safety of a finished cosmetic product, the manufacturer who uses safe ingredients need not retest the final mixture. Cosmetic products are almost always relatively simple mixtures that do not result in chemical interaction or produce new byproducts. When such ingredients are mixed together, there is no reason to believe that the resulting product would be unsafe. This is no different than food. A food manufacturer similarly uses safe ingredients and does not test the final product further. In both cases, the use of safe ingredients, under conditions that do not lead to a chemical reaction, results in an equally safe consumer product. Tests that have been conducted on finished cosmetic products confirm the lack of any synergistic effects that would make them unsafe.

FDA recognizes the fact that mixtures of safe ingredients generally form safe finished products in the way it presently handles OTC drugs. The agency requires the ingredients in such products to be tested for safety, but it does not mandate testing of whole products or testing of combinations of ingredients.

The regulation[36] provides that the fact that an ingredient or product has a history of use in or as a cosmetic does not by itself constitute proof of safety. It specifies that such an ingredient or product may have its safety brought into question at any time by new information even though that information in itself is not conclusive. In that case, the product must carry the safety substantiation warning unless (1) safety was adequately substantiated before the new information was developed; (2) no human health hazard is demonstrated by the new information; and (3) adequate studies are being conducted that will expeditiously determine the safety of the ingredient or product. It clearly states that the existence of these three criteria does not exempt the product from the adulteration provisions or other requirements of the FD&C Act or regulations promulgated under it. Thus, the agency may still take regulatory action against the ingredient or product if it is adulterated.

The safety substantiation regulation provides a strong deterrent to the marketing of any cosmetic that has not been adequately substantiated for safety.

## FDA's Restrictions on Cosmetic Ingredients

FDA has issued regulations banning or restricting the use of a number of ingredients for safety reasons. The agency banned use of vinyl chloride in aerosol cosmetic products due to the chemical's toxicity when inhaled.[37] It also banned use of chloroform in cosmetics.[38] Other ingredients that the FDA has banned or restricted for use in cosmetics include zirconium,[39] bithionol,[40] halogenated salicylanilides,[41] mercury compounds,[42] and hexachlorophene.[43]

FDA has also proposed a ban on use of methylene chloride in cosmetics.[44] Responding to preliminary concerns about the potential risk from this ingredient, most cosmetic manufacturers voluntarily discontinued use of this chemical. Issued in November 1987, the Cosmetic Ingredient Review Expert Panel's Final Report of the Safety Assessment for Methylene Chloride concluded that the chemical "is safe for use in cosmetic products designed for brief discontinuous use."[45] FDA has not yet issued a final order banning use of methylene chloride in cosmetics, but it clearly has adequate authority to do so if the evidence under consideration warrants such action.

In addition to regulating use of ingredients that might cause health-related adverse effects, FDA has authority to regulate ingredients that may pose environmental risks. For example, the agency has banned use of chlorofluorocarbon propellants in cosmetic products because of the reported effects of these compounds on the ozone layer in the stratosphere.[46]

## FDA's Warning Label Regulations

An FDA regulation requires that the label of a cosmetic product "bear a warning statement whenever necessary or appropriate to prevent a health hazard that may be associated with the product."[47] This general regulation is further implemented by specific regulations governing warnings for particular products. For example, the agency mandates a warning about potential skin and urinary tract irritation on bubble bath products,[48] and a general irritation warning must appear on feminine deodorant sprays.[49]

FDA authority to require warning labels relates not only to safety problems associated with product use but also to any problems that may be related to product packaging or consumer misuse. One such regulation requires every cosmetic in a self-pressurized container using a halocarbon or hydrocarbon propellant to be labeled:

> "_Warning_--Use only as directed. Intentional misuse by deliberately concentrating and inhaling the contents can be harmful or fatal."[50]

FDA also requires any cosmetic in a self-pressurized container to carry language warning against such things as spraying the product in the eyes, puncturing or incinerating the container, storing the container at temperatures above 120 degrees, and leaving the product within the reach of children.[51]

Although food, drugs and cosmetics are subject to the FD&C Act and thus exempt from the provisions of the Federal Hazardous Substances Act (FHSA),[52] a regulation issued by the FDA when it had jurisdiction over the FHSA, and now by the Consumer Product Safety Commission, requires the same warnings for FDA regulated products. This regulation provides that such an FDA-regulated product that poses a substantial risk of injury or illness as defined by the FHSA will be misbranded under the FD&C Act unless its label bears information to alert a consumer to the hazard.[53] The misbranding would violate §201(n) of the FD&C Act, based on the manufacturer's failure to reveal a material fact with respect to consequences that may result from use of the product.

## FDA's Inspection Authority

FDA's authority to inspect cosmetic manufacturing facilities enables it to monitor compliance with safety requirements. The agency's Inspection Operations Manual[54] provides FDA inspectors with information on regulatory requirements applicable to cosmetics, including requirements relating to such things as ingredient labeling, restricted ingredients, warning labels, and quality assurance in the production of cosmetics.

The Manual contains information on proper use of some ingredients. For example, it instructs on the permissible levels of formaldehyde in nail hardeners and of mercury compounds in eye area cosmetics.

## The Fair Packaging and Labeling Act

In addition to its authority under the provisions of the FD&C Act, FDA requires cosmetic ingredient labeling under the authority of the Fair Packaging and Labeling Act (FPLA).[55] The FPLA was enacted to give the agency authority, which it did not have under the FD&C Act, to require product labels to provide consumers with information to help them make meaningful comparisons between products.

Regulations issued by FDA under the FPLA require the name of each ingredient to be listed on the outer container of each cosmetic product sold to consumers, whether in stores or in salons.[56] There are only two exceptions:

- The agency may grant trade secret status to an ingredient, which then may be listed as "and other ingredients,"[57] and

- A flavor or fragrance used in a cosmetic may be listed as "flavor" or "fragrance."[58] In its preamble to the ingredient labeling order, FDA stated, "The Commissioner concludes that the listing of all ingredients of fragrances and flavors, each fragrance and flavor perhaps containing twenty or more ingredients, would be impractical and could distract from the listing of other, more significant ingredients."[59] The FD&C Act itself adopts the same approach for the labeling of flavors used in food products.

Detailed FDA regulations govern where and how ingredients must be listed.

## PROFESSIONAL COSMETIC PRODUCTS

### Ingredient Labeling

All cosmetic products sold to consumers -- whether in stores or in salons -- must bear ingredient labeling. As pointed out in previous testimony before this Subcommittee, however, professional products used only in salons are not required by law to be ingredient labeled.

Many manufacturers are reluctant to put ingredient labeling on professional products. This is not because they want to prevent the information from reaching salon workers. It is because such labeling would facilitate diversion of the products to the retail market. Products offered for sale at retail without ingredient labeling are misbranded and in violation of the Food, Drug and Cosmetic Act. Diverted professional products can be identified and removed from the retail shelves if they do not bear ingredient labeling.

Many cosmetic companies have strong programs to combat diversion. They dedicate considerable resources to the task of finding and prosecuting those responsible for diversion of their products.

We object to diversion of professional products to the retail market for two reasons. First, some types of professional products are more concentrated and faster acting than similar products intended for retail sale and use by untrained consumers. An untrained person may not have the skill necessary to apply these products as quickly and precisely as required to achieve the desired results.

In such cases, the consumer may be left with a permanent wave that is too frizzy or with a dramatically unflattering hair color. The reputation of the product's manufacturer would almost certainly be damaged in the eyes of that consumer and others to whom he relates his experience with the product.

Our second objection to diversion is economic. Diversion does economic damage to salons and to professional product manufacturers. Since it is less expensive to launch a new salon product than to launch a new product for the retail market, many professional product manufacturers, like the salons they serve, tend to be small, entrepreneurial businesses. They are particularly vulnerable to the economic injury that occurs when a product that is developed and marketed for use exclusively in salons is subject to unauthorized diversion into the retail market.

Although professional products do not have to be ingredient labeled, their manufacturers have traditionally answered cosmetologists' questions regarding specific ingredients in products. When a professional cosmetic product is associated with an adverse reaction, manufacturers cooperate with dermatologists to evaluate the problem. Cosmetic Industry on Call, a CTFA-published directory of cosmetic company employees responsible for responding to requests for information on cosmetic ingredients and formulations, facilitates such efforts.

Manufacturers of professional products also provide cosmetologists with information through a variety of channels, including through the distributors of the products, through the explicit directions for safe use that accompany products; through material safety data sheets; and through sponsorship of educational programs at trade shows. Moreover, during their schooling, cosmetologists receive instruction on the major ingredients used in professional products.

We support 100 percent communication of information on ingredients contained in professional products. We are exploring ways to make this information more readily available to salon workers without abandoning the industry's fight against product diversion and the problems it brings to consumers, manufacturers, and salons.

Let me stress that although professional products are not subject to ingredient labeling regulations, they are subject to all other FDA regulations relating to safety, including those banning or restricting use of certain ingredients, those requiring premarket safety substantiation, and those mandating product warning labels.

## Workplace Safety Standards

At the July hearing, there was extensive discussion of the health problems suffered by a cosmetology student and a wig stylist. The situations described are tragic. Unfortunately, nothing we can say or do will diminish the problems of these two women. The statements presented by them, however, suggest that the problems they experienced were due to improper working conditions, specifically lack of ventilation, that caused substantial over-exposure to a number of cosmetics, cleaning products, and other chemicals in their workplaces.

Like all chemicals, professional products must be used with proper care in a safe workplace. The Federal Occupational Safety and Health Act[60] provides protection for cosmetologists. The Act, for instance, imposes upon each employer a duty to " . . . furnish to each of his employees employment and a place of employment which are free from recognized hazards that are causing or are likely to cause death or serious physical harm to his employees."[61]

Under the Act, specific airborne exposure limits for the workplace are mandated by the Occupational Safety and Health Administration (OSHA) for most chemicals and the ingredients used in cosmetic aerosols that might be expected to be found in a cosmetology salon.[62] If adequate ventilation is provided to maintain the legally required levels of these chemicals, all other inhalation exposure is minimized as well. Results from epidemiology studies that show cosmetologists are not under increased risks of health effects suggest that the majority of salons are providing safe and healthful workplaces for their employees.

On August 24, 1987, the Hazard Communication Standard issued by the Occupational Safety and Health Administration (OSHA) was extended to cover salon workers.[63] Effective June 24, 1988, the standard requires manufacturers to provide salons purchasing their products with material safety data sheets disclosing specified information on any "hazardous" ingredients.[64] It also requires employers to develop and implement plans to educate and train the work force regarding all hazardous chemicals present in the workplace.[65]

In addition to these federal laws and regulations, state cosmetology laws and occupational safety and health laws also mandate particular workplace hygiene requirements. We know of no state that does not have a law requiring licensing of cosmetologists. These state laws and the regulations promulgated pursuant to them generally require extensive training as a prerequisite to licensure. Properly enforced, these provisions -- which are already on the books -- should be adequate to ensure that professionals have not only the basic knowledge needed to use professional products safely but also a safe environment in which to work.

To illustrate our point, we did some research on Oregon laws. Most of Oregon's statutory provisions governing salon workers are found in the Barbers and Hairdressers Act.[66] This law creates a State Board of Barbers and Hairdressers (the Board) within the Health Division of the Department of Human Resources.[67] The Board has authority to establish and enforce safety standards for the practice of hair design, facial technology, or manicure.[68]

The Assistant Director for Health or a designated representative serves as an *ex officio* member of the Board.[69] The Assistant Director appoints an administrator for the Board[70] and appoints the members of the Board: six certified practitioners and one public member.[71] No member may be directly or indirectly associated in the manufacture of cosmetic supplies or in the distribution of such supplies to licensed practitioners.[72]

To practice hair design, facial technology, or manicure in Oregon, one must have a certificate or permit from the Board.[73] A person who violates this provision:

- Is guilty of a Class B misdemeanor,[74]
- Is subject to administrative sanctions of the Board,[75] and
- Is subject to a civil penalty of up to $1,000 per offense as determined and assessed by the Board.[76]

To obtain a certificate to practice, an applicant must have successfully completed all courses that a school of hair design, facial technology, or manicure must teach in order to be licensed by the state to teach the area of practice in which the applicant wishes to be certified.[77] Oregon's Education and Cultural Facilities Law requires the Board of Education to issue rules requiring each licensed school "to teach, and require for graduation from the school, courses that meet minimum standards set by the board [of Education] on . . . safety for all procedures permitted and in the use of all . . . chemicals permitted within the respective field of practice."[78]

The rules adopted by the Board of Education do require the course of study offered by each school to include instruction on safety and use of chemicals.[79] The rules also require school curriculum and examinations to cover a series of subjects, such as general chemistry; cosmetic chemistry, including physical and chemical classifications, composition and uses; application of cosmetics in keeping with manufacturers' instructions for their use; and safety practices.[80]

In addition to having successfully completed this required course of study, an applicant for certification must have passed an examination given by the Board of Barbers and Hairdressers.[81] The examination must "test the applicant's knowledge of . . . safety for all procedures permitted and in the use of all . . . chemicals permitted within the scope of a license and certificate in the field of practice for which the applicant is seeking certification."[82]

The rules of the Board of Barbers and Hairdressers require each applicant to pass a section of the examination on safety and sanitation and to pass an additional section or sections relating to the type of certificate (hair design, facial technology, or manicure) sought.[83] All sections test the applicants' knowledge of basic principles of safety and of chemicals used.[84]

The Board of Barbers and Hairdressers may waive these educational and examination requirements only under specified limited conditions where it determines that the applicant has met substantially equivalent requirements in another state or territory.[85]

In addition to governing the training and qualifications of practitioners of hair design, facial technology, and manicure, Oregon laws and regulations govern the operation of shops and schools. For example, the Board of Barbers and Hairdressers is authorized to issue rules prescribing safety requirements for cosmetology and barber shops.[86] A copy of these rules is furnished to the owner or manager of each shop.[87] To obtain a license to operate, a shop must comply with the Board's rules on health and safety as well as with applicable health and safety laws and rules of the Health Division and other state agencies.[88]

The Board of Barbers and Hairdressers has issued safety rules for shops. Among other things, these rules require chemicals to be mixed in a dispensing area that has adequate ventilation.[89] The rules define "adequate ventilation" as "ventilation by natural or mechanical means sufficient to exhaust hazardous or objectionable fumes or vapors, and to allow the free flow of air in a room in proportion to the size of the room and the capacity of the room."[90] The Board has also issued a regulation governing safe storage of chemicals.[91] In addition, to provide further guidance to practitioners, the Board has issued an extensive Practitioner Handbook, which describes such things as the chemical composition of, and storage and handling precautions that should be taken in connection with, chemical products commonly used in the cosmetology profession.[92]

Oregon law authorizes the Board of Education to adopt any rule it considers necessary to protect the physical health and safety of students attending schools teaching hair design, facial technology, or manicure.[93] The Board of Education has adopted a rule requiring schools to comply with specified sections of the shop safety rules issued by the Board of Barbers and Hairdressers, including those sections requiring chemicals to be mixed in a dispensing area that has adequate ventilation and those sections governing safe storage of chemicals.[94]

Both shops and schools are subject to inspections for compliance with statutory and regulatory sanitary and safety requirements.[95] The Assistant Director for Health is required to establish an inspection program within the Health Division.[96] Board of Barbers and Hairdressers regulations require shops to allow inspections when they are open for business[97] and to post inspection certificates in public view.[98] Board of Education regulations require any violation found during a school inspection to be reported to the State Superintendent of Public Instruction.[99] A school's failure to correct a violation within the time allotted for compliance as determined by the Superintendent would subject the school to penalties,[100] including license suspension or revocation and civil fines of from $300 to $500.[101]

In addition to laws specifically relating to the practice and teaching of hair design, facial technology, and manicure, Oregon's Safe Employment Act includes general provisions on employment safety that apply to salons. The law requires employers to furnish employment and places of employment that are safe and healthful; to adopt practices and operations that are reasonably necessary to make the employment and place of employment safe and healthful; and to do "every other thing reasonably necessary" to protect employee life, safety, and health.[102] The Safe Employment Act is enforced by the Director of the Oregon Department of Insurance and Finance.[103] The Director is also authorized to enforce all regulations, rules, and standards adopted by other state agencies for the safety and health of employees.[104]

The point is, existing Oregon laws and the regulations promulgated under their authority:

- Require persons licensed to practice hair design, facial technology, and manicure to be trained to handle professional cosmetic products safely.

- Require salons and schools to be safe and to pass safety inspections.

If properly enforced by Oregon officials, these provisions will give the state more than adequate authority to protect the health and safety of salon workers. We support these laws and regulations. We want our safe products to be used safely in a safe environment.

Professional Product Safety

Most of the ingredients used in professional products are the same as those used in retail products sold to consumers; therefore, our earlier testimony documenting the safety of cosmetic ingredients and products applies equally to retail and professional products. In general, any differences in formulation of professional products focus on increasing the concentrations of ingredients, using faster acting ingredients, and preparing products in bulk or as concentrates for dilution by the cosmetologist.

Added to the safety assurances provided by the CIR Expert Panel on individual ingredients, as well as other data presented above, there are well documented epidemiology studies that demonstrate that, overall, there are no significant increased health risks associated with the occupation of cosmetology.

Respiratory Data

Available epidemiology data do not establish a causal relationship between a cosmetologist's exposure to professional products and asthma or other respiratory diseases. In a survey conducted by the National Institute for Occupational Safety and Health (NIOSH) during 1977 and cited by the UFCW in its July testimony, the authors compared a small sample of student cosmetologists and practicing beauticians with a group of subjects matched for gender, age, smoking history, and geographic location.[105]

In evaluating a questionnaire designed to elicit the prevalence of respiratory symptoms, such as cough, shortness of breath, and wheezing, it was determined that cosmetologists had a higher prevalence of complaints, although this was shown only for the group less than 40 years old. The expected increased prevalence of symptoms in smokers versus non-smokers or ex-smokers was not observed.

Results from tests given to evaluate pulmonary function, and chest x-rays, did not show a significant difference between the cosmetologists and the control population, although the authors stated that there was a suggestion of a trend toward small airway obstruction with increasing years of exposure in small-salon employees only. Two years later, a follow-up by the same primary authors showed that there was "no support for the concept that there is a specific infiltrative pulmonary disease which results from the inhalation of hair spray."[106]

Another study, which was sponsored by CTFA in 1979, compared more than 900 cosmetologists to a matched control group of telephone workers.[107] The reported findings largely supported the results of the initial study by NIOSH, in that the cosmetologists had a greater prevalence of respiratory complaints, but there were no significant differences in pulmonary physiologic measurements or chest x-ray findings. In this study, in addition, there was no difference between cosmetologists employed for less than seven years and those employed for more than seven years. The study also failed to show any association of pulmonary function trends with work in small salons.

Finally, a large study by the American Cancer Society, which was conducted from 1959 to 1978 and which included information on 5,125 beauticians, concluded there was no disease for which the cosmetologists had a higher death rate.[108]

## Central Nervous System Disorders

Although case reports and anecdotal information may claim a link between professional product use and central nervous system disorders, we are not aware of any epidemiology data that suggest an association between the two. As we noted above, OSHA has promulgated regulations limiting airborne concentrations of most organic vapors and gases in the workplace to protect employees from both the acute and chronic effects of over-exposure. In addition, groups such as NIOSH and the American Conference of Governmental Industrial Hygienists (ACGIH) have proposed workplace limits on exposure to many other compounds. When these national and state regulations on workplace safety and hygiene are followed, salon employees are safe.

## Mortality/Cancer

Many of the studies attempting to determine whether cosmetologists are under an increased risk of death from cancer or other disease suffer from the common problems of lack of control for confounding factors, lack of statistical power, or both.[109] For the most part, the studies cited at the July hearing made use of data from cancer registries, which record only cancer site and occupation, and no additional information. As pointed out in a working paper for the International Commission for Protection Against Environmental Mutagens and Carcinogens, "Without specific information on habits like tobacco smoking, it is impossible to decide whether any increase in cancer . . . is occupational or attributable to lifestyle."[110]

In this context, "lifestyle" includes such factors as active or passive smoking, alcohol consumption, diet, socio-economic class, parity, age at first pregnancy, and sexual promiscuity. Each of these factors is known to affect the chance of developing one or more specific types of cancer, but they have not been taken into account in most of the studies relating to cancer in cosmetologists and hairdressers.

There have been three major epidemiology studies examining mortality/cancer incidence in cosmetologists.[111] In each of these, the data demonstrated no causal relationship between overall cancer, or cancer at any particular site, and the occupation.

One study was conducted by the American Cancer Society.[112] This lifestyle study on over 100,000 people followed a subset of 5,125 beauticians over a 13-year period. In this population, compared to non-beauticians matched on age, race, education, place of residence, amount of cigarette smoking, past history of cancer, and past history of heart disease, the results showed death rates slightly lower in the beauticians than in the controls. The results also showed that there "was not a single site of cancer from which significantly more beauticians than non-beauticians died."

In a study which followed 7,736 Japanese female beauticians between 1953 and 1977,[113] no measurable excess mortality was noted for any site of cancer, except that stomach cancer was significantly elevated. It was explained in the paper that the excess stomach cancers, 15 cases more than expected, might be due to other factors, such as diet, that are closely connected with stomach cancer. The study also noted no additional excess mortality from tuberculosis, heart disease, or accidents.

In the largest study reported to date,[114] which was supported by the National Cancer Institute, NIOSH, and CTFA, 13,650 Connecticut cosmetologists were compared with the general Connecticut population for cancer mortality during a 44 year period. Smoking data and reproductive history was not available, limiting the evaluation of the results. The only significant finding reported in the study was an association between respiratory, breast, corpus uterine, and ovarian cancers in female cosmetologists who entered the profession between 1925 and 1934. The authors state, "Occupational risk seems unlikely as an explanation for the cancer excess in the 1925-34 entrants." The authors concluded that their results for females who began work after 1935 were consistent with the American Cancer Society survey and the study of Japanese beauticians discussed above.

A 1985 review of the epidemiology, which appeared in a publication of the International Agency for Research on Cancer, concluded, "No specific cancer has consistently been found to be increased in incidence among hairdressers and beauticians."[115]

## Dermatitis

We have reviewed earlier in our testimony a number of sources of data on the incidence of cosmetic adverse reactions, which consist mostly of dermatitis, and properly concluded that the risk from use of cosmetic products is well within an acceptable range. Based on the assumption that cosmetologists will use professional products properly and with common sense to protect their skin from drying or damaging products, we believe professional use of cosmetics products will be equally safe.

## Conclusion

While thousands of cosmetologists assist their clients in the application of professional products successfully and with no ill effects, some cosmetology salon workers undoubtedly do have adverse reactions to professional products. Some part of the cosmetology population, like some part of the general population, will react adversely to every chemical that exists.

These reactions, while generally mild and temporary, are unfortunate -- all the more so because they may in some instances affect the ability of the worker to function in his or her chosen profession. At the same time, though, this is not a situation unique to the cosmetology profession. For example, we know of one very bright young woman who had to give up her dream of being a veterinarian because of her adverse reaction to products routinely used to wash animals. There are also cases of printers who react adversely to chemicals used in inks. Such situations are tragic, but they are not the fault of the products or of their manufacturers. It is a sad fact of life that the inherent physiological characteristics of some people unavoidably preclude them from engaging in some professions.

Professional products are safe for the overwhelming majority of salon workers who are properly trained; who handle the products with the respect that common sense dictates must be given any chemical product -- from aspirin to household cleansers; and who use the products according to the manufacturers' directions for safe use. Intentional or careless misuse of a product, however, is unsafe. For example, exposure to any volatile chemical for long periods of time in enclosed, inadequately ventilated areas will result in health problems.

## SKIN CARE PRODUCTS

### FDA's Authority Over Skin Care Products

The FD&C Act gives FDA authority to regulate the label and labeling of all cosmetic products. Section 602(a) provides that a cosmetic is misbranded if its labeling is false or misleading in any particular.[116] Thus, the agency has adequate authority to regulate claims for all cosmetics, including skin care products, under the existing law.

FDA has exercised that authority vigorously. Since 1987, the agency has written 24 regulatory letters relating to claims made in connection with such products. It has also issued an import alert and a field directive ordering its border and other field offices to be on the lookout for products whose labeling may be in violation of the FD&C Act. If FDA believes that skin care products should be regulated as drugs, it clearly has demonstrated that it has the authority to proceed.

The safety of skin care products has not been called into question. As Dr. Gary Grove said in testimony to the Subcommittee at its July 14 hearing, "It is important to note that in this recent flurry of FDA activity, the safety of these [skin care] products was not an issue. This is not surprising since most cosmetic companies do considerable pre-market testing to establish the safety of their newly created products. Indeed the industry should be praised for the approach it has taken to self-regulation since it works so well."[117]

FDA has more than adequate authority to ensure the proper labeling and continued safety of skin care products. These products are subject to the same array of statutory and regulatory safety requirements that apply to other kinds of cosmetics.

## Federal Trade Commission Authority Over Skin Care Claims

In addition to the requirements of the FD&C Act, cosmetics -- including skin care products -- are regulated by the Federal Trade Commission (FTC).[118]

Provisions of the Federal Trade Commission Act specifically prohibit the use of false advertising claims for food, drugs, devices, and cosmetics.[119] A "false" advertisement is defined to include claims that fail to disclose material facts.[120] The Act also prohibits unfair or deceptive advertising.[121] This has been interpreted to require advertisers of consumer products to have sufficient information on file to substantiate their claims. The point is, the FTC has authority to take action against product claims when appropriate.

Many individual states have passed similar laws, which are actively enforced by state attorneys general.

## The National Advertising Division

A private sector group, the National Advertising Division (NAD) of the Better Business Bureau, also investigates the veracity of advertising claims for cosmetics. The NAD was created in 1971 by the American Advertising Federation, the American Association of Advertising Agencies, the Association of National Advertisers, and the Council of Better Business Bureaus. Its goal is "to help sustain high standards of truth and accuracy in national advertising to the benefit of the consumer and thereby enhance the reputation of the [advertising] industry."[122]

The NAD reviews advertising claims to determine whether they have been substantiated. A number of things can trigger an NAD review, including challenges from competitors of the company making the claim and consumer complaints. If it finds that a claim has not been substantiated, NAD asks the advertiser to alter or withdraw advertisements containing that claim. The advertiser can appeal to the National Advertising Review Board; however, only about two percent of NAD cases are appealed.

## THE DETRIMENTAL IMPACT OF OVER-REGULATION

### Impact on Small Businesses

No amount of regulation will totally eliminate all adverse reactions to cosmetics, or to anything else. Excessive regulation would, however, have a negative impact on the cosmetic industry, especially small businesses. The products manufactured by these businesses are safe. Industry programs, such as CIR, and publications, such as the CTFA Technical Guidelines, help them comply with legal and regulatory requirements and assure product safety. Additional -- unnecessary -- requirements, however, could well.drive small companies out of the marketplace.

In the words of Commissioner Frank Young, "FDA's goal is always to protect the public -- sensibly. We always want to avoid risks to the public, yet we don't want to hamper growth and innovation with unnecessary regulation. Safety policies, whether for foods, drugs or cosmetics, must be rational and grounded in good science."[123]

### Impact on Governmental Resources

It is neither feasible nor desirable for the government to regulate extensively every product and every facet of life. Public policy and finite resources demand that legislators and regulators set their priorities carefully -- that they regulate only those things that truly require regulation.

As expressed by former FDA Acting Commissioner Sherwin Gardner in 1979:

> "There is no practical application of absolute safety. Moreover, we all have to deal with the fact that our resources for coping with problems are limited. . . . We do, however, need a rational allocation scheme to apply resources for the purposes of reducing risks and for developing new products to meet new needs. We do need to be able to set safety standards in a way that would allow the selective application of resources to the problems most deserving of attention."[124]

We must set our priorities and allocate our resources wisely. The Congress should resort to added regulatory requirements only when the record clearly demonstrates that they will have a positive impact on public health. No such record of need can be established in the case of cosmetic products. Existing programs are quite sufficient to protect public health.

Here is what some recent FDA commissioners have said about the relative safety of cosmetic products:

> Commissioner Frank Young has said that "cosmetics are, in general, less likely to cause harm than the other products FDA regulates."[125]
>
> In the words of former Commissioner Arthur Hull Hayes, Jr.: "When we compare the health and safety issues associated with food, drugs, medical devices and cosmetics, I am sure we can all agree that cosmetics, by virtue of their composition and use, are in general less likely to cause concern for harm than the other products the agency regulates."[126]
>
> As former Commissioner Alexander Schmidt said at congressional hearings in 1974, "When viewed in the context of FDA's total consumer protection responsibilities, we would, in general, rank questions concerning cosmetic safety lower in priority than food, drug, device, or radiation safety."[127]
>
> Commissioner Schmidt later expanded on that statement as follows: "The sum of all known, reported and suspected problems of cosmetic safety

do not add up to anyone's first priority when compared with most other safety issues before society. On the basis of present knowledge, it seems clear that in terms of FDA's total responsibility for consumer protection, cosmetic safety ranks lower than our other priorities for foods, drugs, medical devices and radiation protection."[128]

Increasing regulation of cosmetic products, which are already well regulated and very safe, would senselessly divert precious government resources from truly important health problems, such as AIDS.

### Impact on Scientific Resources

Imposition of additional, unnecessary requirements on the cosmetic industry could require an extraordinary commitment of scientific resources. For instance, mandating additional testing for cosmetics would without a doubt result in a significant, needless increase in the number of laboratory animals required. This would come at a time when elimination of all unnecessary uses of laboratory animals is a goal of major importance to the cosmetic industry as well as to many animal rights groups and members of the public. In fact, the cosmetic industry continues to be a leader in the search for reliable safety substantiation methods that can replace animal testing. For example, CTFA and its members have created and support two major research programs seeking alternatives to animal testing. One is located at Battelle's Columbus Laboratories. The other, at the Johns Hopkins University, Center for Alternatives to Animal Testing. Many individual cosmetic companies make significant additional contributions to other, similar efforts.

## CONCLUSIONS

From the evidence presented, we draw three important conclusions:

1. Cosmetics are beneficial products with an exemplary safety record of which we are justifiably proud.

2. The cosmetic industry has voluntarily undertaken a variety of highly-regarded and effective safety programs.

3. FDA has and exercises adequate authority to regulate cosmetic products.

We firmly believe that additional regulation of cosmetic products is not only unnecessary but also would adversely affect both the industry and the nation's governmental and scientific resources.

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# STATEMENT OF
# FRANK ROMANO
## CHAIRMAN AND CEO
## KEY WEST FRAGRANCE AND COSMETIC FACTORY, INC.

BEFORE

THE SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

OF

THE COMMITTEE ON SMALL BUSINESS OPPORTUNITIES

U.S. HOUSE OF REPRESENTATIVES

September 15, 1988

Good morning, Mr. Chairman and members of the subcommittee. My name is Frank Romano. I am Chairman and CEO of the Key West Fragrance and Cosmetic Factory. I started the Company on a shoestring some seventeen years ago in a tiny 800 square foot space. My first day's sales were all of $36. We were doing something right, because with luck and a lot of hard work we have become very successful.

From our modest beginnings in Key West, Florida we have branched out through retail and catalog sales to all parts of the country, including Hawaii where we have several stores. We manufacture and market a wide variety of products, including skin care, suntan, hair, bath, men's products and fragrances. Our products are formulated and manufactured in our own manufacturing facility adjacent to our Headquarters store in Key West.

Mr. Chairman, I invite you to come to Key West to inspect my facility. Every single day we have the public enter and watch our factory at work. I am confident, Mr. Chairman, that you will be impressed with the quality of its operations, and the high standards we follow in manufacturing our products. As a small businessman, I am very grateful for the opportunities this country's free enterprise system has given me. And I am most concerned that my company's products continue to live up to the high standards that my customers have come to rely upon.

I must be candid with you, however. I am alarmed about the atmosphere that surrounded the hearing held here in July. The cosmetic industry, of which I am a member, takes pride in the safety of its products. But isolated incidents are being used to needlessly frighten the American consumer. Some of the witnesses at the last hearing in July seemed determined to use them as an excuse to saddle the industry with additional, unnecessary regulations.

Mr. Chairman, I want to assure you that my company observes the highest quality performance standards in manufacturing our products. We use proven ingredients that have been substantiated for safety and have stood the test of time. We test every ingredient upon delivery. Our facilities are inspected at both the federal and the state level. I just had a State of Florida inspection last month. We passed with flying colors! Believe me, I can tell you from personal experience that both state and federal cosmetic safety laws are more than adequate to ensure safe products for our customers. What's more, our safety record is outstanding. Our product complaint record is infinitesimal. I have never had a lawsuit about my products in the entire seventeen years of operation. I have never had a serious complaint. We can point with pride to millions of satisfied customers. I might add that our company supports, and fully participates in, the FDA's voluntary cosmetic reporting program.

Imposing unnecessary new regulations on my Company simply does not make sense. Why should I spend money to re-test proven ingredients that we know are safe? Why should my customers pay for this unnecessary testing? Why should some of my colleagues in the industry not be able to compete with large manufacturers -- or worse yet, risk being put out of business because of a new and unnecessary regulatory scheme? Why should this country's testing resources be diverted from more important health concerns? Why should more animals be sacrificed to re-establish the safety of proven ingredients?

The cosmetic industry must anticipate and react quickly to changing tastes in fashions and styles. Unwarranted new regulations will cripple our ability to respond in a timely fashion. Millions of women customers will be made unhappy.

Unlike the large companies in our industry, we small businessmen cannot spread our costs over many millions of sales units. Speaking for myself, and on behalf of my small business colleagues in this industry, I urge you not to hamper an important part of America's economy by imposing needless, new regulations. Thank you, Mr. Chairman.

SUBCOMMITTEE ON REGULATION AND BUSINESS OPPORTUNITIES

DATE AND TIME: Thursday, September 15 at 11:00 A.M.

PLACE: Room 2359A Rayburn House Office Building

ICMAD (Independent Cosmetic Manufacturers and Distributors, Inc.), a non-profit trade association representing more than 500 smaller companies in the cosmetic industry

Witness List: Jerome N. Michell, Executive Director, ICMAD

Winnie Baden, President, Rose Laird Cosmetics and Board Member, ICMAD

Hal Lightman, President, I.S. Laboratories, Inc. Founding Member and former President, ICMAD

ICMAD Legal Counsel: Walter E. Byerley

Remarks by Jerome H. Michell, ICMAD Executive Director

Congressman Wyden, members of the committee, ladies and gentlemen. Thank you for inviting our association to participate in this hearing covering cosmetic safety. My name is Jerome Michell and I am Executive Director of the ICMAD, the Independent Cosmetic Manufacturers and Distributors, founded in 1974, a non-profit trade association of more than five hundred cosmetic companies located in thirty five states. It is estimated that there are approximately 2500 cosmetic manufacturers and distributors in the United States. Thus, ICMAD membership accounts for roughly 20% of these cosmetic companies.

ICMAD is entrepreneurial in character, representing primarily small business ownerships versus the public ownership of the major cosmetic companies. May I call your attention to the packet you have received which contains nine pertinent informational pieces concerning cosmetic and ICMAD activities.

I would like to introduce two of our Board Members to present their individual thoughts about cosmetic safety in our industry; Winnie Baden of Rose Laird Cosmetics and Hal Lightman of I.S. Laboratories, one of our founders and a past president of ICMAD.

Remarks by Winnie Baden

Congressman Wyden, members of the committee, I am Winnie Baden, President of Rose Laird Cosmetics, a company in continuous commerce selling many millions of skin and hair care products since 1912. Prior to 1968, we sold our products to better department stores and in our salons on Fifth Avenue and Park Avenue. For the last 20 years we have sold through direct mail.

Rose Laird, like many other cosmetic companies, does not make its own products. We do however, have our own formulas, and we oversee the manufacturing and personally test each new batch.

From personal experience, during my six years as a Board Member of ICMAD, I have found that our membership represents concerned individuals who wish to provide the purest, safest products at the most economical prices. We are all, in addition, very dependent upon the look, the feel, and the effectiveness of each and every product. Everyone in the cosmetics and personal care industry is truly concerned about the products we place on our faces, on our hair and on our bodies. We all use these products, and we all police ourselves as individual manufacturers, distributors and consumers in order to keep industry products safe.

One of the purposes of a trade organization, such as ICMAD, is to provide its members with an opportunity to share their experiences and knowledge about reputable private label companies who employ competent cosmetic chemists, and insist on good manufacturing practices, and test final formulations. These practices include the use of approved ingredients, microbiological testing of each batch and skin testing for possible reactions.

ICMAD's members are primarily smaller cosmetic companies who do not have the legal and technical staffs of the larger companies. ICMAD makes certain, therefore, that members promptly receive new, relevant information as it becomes available. Professional assistance is provided through our legal counsel, intra-association "hot" line, monthly informational publications and bulletins that cover every critical issue, whether it affects just one member or the entire industry.

Since 1983, ICMAD has worked closely with the FDA in co-sponsoring a continuing series of Cosmetic Educational Workshops. Our joint purpose has been to keep smaller companies informed and up-to-date on all regulatory and legislative matters. Attendance has been excellent. More than 100 companies have enthusiastically attended each seminar. On November 1st, 1988, we will co-sponsor with the FDA our ninth workshop in New Orleans. These seminars have previously been conducted in New Jersey, Florida, Texas, Illinois and California. Copies of our printed matter and workshop agendas have been provided the committee.

The documents this committee has accumulated, and the figures which have been extrapolated all indicate that the issue is not the safety of the products which the cosmetic industry manufactures for the retail market, but rather how the products are professionally used in the workplace and how products to be used by professionals only should be labeled.

Over the years a mass of data has accumulated which clearly places cosmetics among the safest consumer products on the market. This is particularly sc considering the number of consumers, the frequency of cosmetic use, and the very low percentage of insurance claims filed. Rose Laird for example among its more than 300,000 clients has had no adverse reactions reported for the past 50 years.

ICMAD believes that every effort should be made to improve the working conditions of beauty professionals who are exposed to certain chemicals almost every day of their lives. It should be assured that, as professionals, they have been instructed on the nature of their industry products, and how, and where to use them. Beauty professionals should receive instruction on the flammable nature of many of the products they use professionally, and the need to prohibit smoking within their work environment, and also because cigarettes are considered a carcinogen.

ICMAD supports the use of ingredient disclosure for all products sold for professional use in the beauty industry. Appropriate warnings clearly printed on labels are already mandatory. OSHA already has mandatory standards for beauty salons, and these standards can and should be enforced by the Board of Health in every community.

ICMAD maintains that further restrictions on the cosmetic manufacturing community would only promote a hardship for small business owners. For every manufacturer in the industry - large, medium and small - the financial cost to implement additional changes, as has been proposed, would lead to price increases on products that already are becoming out of reach. These restrictions would, in addition, severely burden the small business segment of the cosmetic industry, and without a doubt, shrink the number of entrepreneurs, the lifeblood of our association, and of our country.

Thank you.

Remarks by Hal Lightman

Congressman Wyden, members of the committee, my name is Hal Lightman. Fifteen years ago, I was one of the founders of ICMAD and have spent 30 years in different facets of the cosmetic field. At present, I am president of I.S. Laboratories, a small family-owned cosmetic company.

In 1974 - 11 concerned men and women - all owners of small cosmetic businesses who believed in the American Dream - formed the Independent Cosmetic Manufacturers and Distributors to represent them and protect the small entrepreneur's interests. These original 11 have grown so that today ICMAD represents more than 500 member companies in over 35 states - including minorities, blacks, mexican-americans, asiatics, spanish-americans, single parents, veterans and senior citizens.

ICMAD members have available to them, in many instances, the same technical sources to protect the public health as the major publicly-owned cosmetic companies. All of us have the results of toxicity testing on ingredients, and we all use only those ingredients found to be safe. Many use the same laboratories for testing finished cosmetic products, including microbiological testing, batch and challenge testing. I have personally used the same testing laboratories for this type of safety testing of cosmetic products as do the giants of the industry.

The smaller entrepreneur - in addition to government regulations - has other great incentives to produce safe products - namely to protect his customer and to avoid product liability exposure. In today's litigious climate, any manufacturer would be a fool not to comply with all federal regulations. If proper record keeping and housekeeping practices are not followed, a company's very existence is jeopardized.

Everyone agrees that there is no such thing as a "zero-risk" product. Everyone accepts that somewhere, sometime, someone will experience a skin reaction in her or his use of a cosmetic. And, of course, we are concerned about every incident, but more regulations will not prevent the misuse of or allergic reactions to any product. ICMAD feels that current FDA regulations covering the cosmetic industry are more than sufficient to protect the public.

Many of our members are beginning to export for the first time - which can help reduce the balance of payments, the deficit and create new jobs - but this will be strangled by unnecessary additional regulation - as would our very existence.

ICMAD would like to note that the testimony of the two cosmetologists who appeared before the committee on July 14, 1988 actually dealt with poor ventilation. We deplore the working conditions, that these workers described and applaud the union if they brought these experiences to OSHA for remedial action. That is, of course, where they would and could solve the problem as described.

However, we trust the committee will disregard the other statements of Beth Shulman, Vice President of Professional Hair Care and Beauty Trades - which were unfounded. These allegations about the entire cosmetic industry - unsubstantiated by facts - we deplore. They question the integrity of our many small business entrepreneurs. They are extravagant and biased and we feel certain the committee will see them for what they are - simply "Headline Seeking." ICMAD deplores the seizing upon isolated incidents to brand an entire, safe industry as dangerous and irresponsible.

ICMAD urges the committee to place the testimony given by previous witnesses and alleged injury statistics they extrapolated in true perspective against the broad safety record and actual experience of the entire cosmetic industry. We support existing FDA requirements and we follow them. We join CTFA in supporting a program to provide ingredient information in beauty salons for professional products.

Finally, we repeat, ICMAD and its individual members are totally committed to protecting the consumer. ICMAD and its individual members are firmly opposed to any additional restrictive legislation that increase the costs of our products - without benefit - to the consumer. That threatens the survival of the small cosmetic companies.

ICMAD as an association of small cosmetic businesses is prepared to offer its full cooperation to the small business subcommittee in its efforts to protect and insure product safety in the workplace and in the home.

Please - do no be like the friend who put a tourniquet around his associate's neck to stop a nosebleed.

Thank you.

AHBAI
THE PROUD LADY

**Board of Directors**
**Officers**
*Chairman*
Gary Gardner
Soft Sheen Products Co.
*1st Vice-Chairman*
Fred Luster
Luster Products Co.
*2nd Vice-Chairman*
Nathaniel Bronner, Sr.
Bronner Bros.
*Treasurer*
Frank Davis
Worlds of Curls, Inc.
*Secretary*
Joe L. Dudley, Sr.
Dudley Products Co.
*Parliamentarian*
William Nelson
Gentille Products Co.
*Historian*
A.W. Curtis
A.W. Curtis Labs
*Past Chairmen*
George Johnson 1981-83
Johnson Products Co., Inc.
Cornell McBride 1983-85
M & M Products Co.
Comer Cottrell 1985-87
Pro-Line Corporation
*Members*
Alaton Products
Charles Brown
Sir Charles, Inc.
Chapman R. Cannon, Jr.
American Beauty Products Co., Inc.
Edward Gardner
Soft Sheen Products Co.
Ernest Jenkins
J.M. Products Co.
Stephen G. Luster
Chemco Laboratories
Thomas McKenzie
M & M Products Co.
Ray Randolph
Madame C.J. Walker Mfg. Co.
Joyce Steele
American Caribbean Beauty Products
Al Washington
AFAM Concepts, Inc.
Jerry White
Kizzi Professional Products
Wesley Wilborn, M.D.
W & W Pharmaceuticals

*Executive Director*
Geri Duncan Jones

# STATEMENT

# OF THE

# AMERICAN HEALTH AND BEAUTY AIDS INSTITUTE

SUBMITTED TO THE

REGULATIONS AND BUSINESS OPPORTUNITIES SUBCOMMITTEE

COMMITTEE ON SMALL BUSINESS

U.S. HOUSE OF REPRESENTATIVES

OCTOBER 5, 1988

**American Health and Beauty Aids Institute**
Headquarters · 111 E. Wacker Drive · Suite 600 · Chicago, Ill. 60601 · Phone: 312-644-6610
TELEX: 25-4073 · FAX: 312-565-4658

The American Health and Beauty Aids Institute (AHBAI) is pleased to have this opportunity to submit its views on your Subcommittee's examination of the potential health hazards of certain cosmetic products. The American Health and Beauty Aids Institute is a national trade association of ethnic health and beauty aids product manufacturers, headquartered in Chicago, Illinois. This statement will be confined to an overview of the Institute's membership, an explanation of the membership's role in the cosmetic industry and society as a whole, and an analysis of the steps taken to insure product safety by the Institute's members.

Founded in 1981, AHBAI's mission is to promote the image and development of the ethnic health and beauty aids industry; represent its member companies and industry interests before legislative and regulatory forums; foster communication between member companies and allied associations, suppliers, retailers, professional cosmetologists and consumers; and, to contribute to the economic development of minority communities.

The membership of the AHBAI is composed of 20 minority-owned manufacturing companies (many of which are small businesses) located in cities across the United States. Combined, these companies account for approximately $250 million in annual product sales, roughly 25 percent of the total $1 billion retail ethnic hair care market. As minority-owned business enterprises with a deep commitment to the economic stability of their communities, AHBAI member companies reinvest profits in a variety of civic and economic development activities, including providing over 3,000 jobs nationwide, college scholarships, and other forms of philanthropy for the purpose of enhancing the quality of life within minority communities across America.

For example, AHBAI sponsors the nationwide "Black on Black Love" Campaign to help promote a greater awareness of positive mental image and self-esteem while urging a reduction in crime in minority neighborhoods. An extensive advertising and public relations effort has been launched to mobilize the support of business, community organizations, government and concerned citizens.

In 1986, Afro-American consumers purchased $2.7 billion in toiletries and cosmetics, according to an independent marketing research organization. Of this total, 42.7 percent went to retail purchases of hair care products.

The 20 member companies of AHBAI, as previously stated, account for about 25 percent of retail hair care product sales. The balance of the business is held by a diverse group of minority and general market companies, including Revlon, Alberto Culver, Clairol, and Keystone Laboratories.

There are six major product categories within the ethnic retail hair care market: hair relaxers, cold wave curl kits, hair sprays, comb easy lotions, conditioners and hair dressings and curl maintenance products. There are dozens of competing products in each of these product categories, regionally and nationally. Products are available for sale in nearly 20,000 retail outlets across the country, including drug, mass merchandise, food and barber and beauty supply outlets.

The AHBAI member companies are progressive and responsible business organizations that share a long and proud history of achievement and product innovation. From AHBAI companies have come virtually every significant new product breakthrough within the ethnic beauty care industry over the past three decades. Numerous technical and scientific procedures are routinely used to ensure the highest standards of product quality and consumer safety. Our companies devote millions of dollars each year to product research and development. Quality control, throughout all phases of the manufacturing process, comprises the cornerstone of each AHBAI member company's efforts.

In addition to the industry's ongoing safety research and testing for retail products, we also promote the safe use of our wholesale products by hair care professionals through detailed educational instructions and product knowledge training seminars.

During a recent hearing before your committee, allegations were made regarding curl maintenance products, inaccurately referred to in the testimony as "jheri curl" products. These charges resulted from a tragic accident involving a consumer who claimed that a curl maintenance product caused the flammability of her hair to increase following application. While we regret deeply the injury caused to any consumer, please note that this references only an isolated incident out of millions of consumers who use these products yearly with safety and confidence.

According to our research, approximately 70 million units of curl maintencance products were sold at retail outlets, from 1983-1986. We in no way believe that this incident should call into question the safety of these products.

The members of AHBAI believe strongly that the most commercially successful products are ones which consumers know and trust. The products sold by our members meet this criteria -- due in large part to the extensive product safety research and testing that takes place before products are marketed to consumers. For example, the product involved in the unfortunate accident mentioned previously, had been tested by the manufacturer for such things as skin and eye irritency -- as well as the level of flammability -- prior to its introduction into the market. These tests showed the product to be safe. Moreover, the two product ingredients identified in the testimony -- glycerine and propylene glycol -- have been commonly used in a variety of different hair care products both in the ethnic industry and the general market health and beauty aids industry.

Nevertheless, due to the fact that hair, itself, is flammable, this particular product carries a warning label (a voluntary effort on the part of the manufacturer) urging that hair be kept away from open flame. AHBAI companies believe that this is a responsible  and further safeguard for consumers.

In summary, AHBAI believes that the industry's voluntary product safety testing and labeling, in conjunction with existing federal regulatory authority over health and beauty aids products, has created an effective mechanism for assurance of safety in the use of our products by the public. Moreover, given the existence of self-regulatory programs in the industry, we believe further federal regulatory authority is unwarranted.

Please be advised, however, that AHBAI companies are reviewing and will continue to review their product safety testing standards and procedures to ensure that they remain consistent with the companies' commitment to producing products of the highest quality and safety.

We thank you, Mr. Chairman and members of the Subcommittee, for this opportunity to present our views on an issue of critical concern to American consumers, as well as our industry. Please call on AHBAI whenever we may be of assistance to you.

COSMETIC INGREDIENT REVIEW

C I R

September 27, 1988

The Honorable Ron Wyden
Chairman
Regulation and Business
  Opportunities Subcommittee
House Committee on Small Business
Room B-363
Rayburn House Office Building
Washington, D.C.  20515

Dear Mr. Wyden:

Please find enclosed various documents for inclusion in the record of your September 15 hearing on the cosmetic industry. These documents include the following:

1) Statement of Dr. William Berndt, Chairman of the Cosmetic Ingredient Review Expert Panel;

2) Statement describing the procedures of the Cosmetic Ingredient Review; and

3) the CIR Final Report for Methylene Chloride.

Sincerely yours,

Robert L. Elder, Sc.D.
Director - CIR

0441Ca

1110 Vermont Avenue NW Suite 810 WASHINGTON, DC 20005 202•331-0651

September 1, 1988

Congressman Ron Wyden
Subcommittee on Regulations
  and Business Opportunities
Committee on Small Business
House of Representatives
1406 Longworth House Office Building
Washington, D.C. 20515

Dear Congressman Wyden:

As the Chairman of the Cosmetic Ingredient Review's Expert Panel I would have preferred to present my views on this program in person; however, my responsibilities as Vice Chancellor for Academic Affairs and Dean for Graduate Studies and Research at the University of Nebraska Medical Center make that impossible. Therefore, I would like to take this opportunity to send you my thoughts on the Cosmetic Ingredient Review Expert Panel and its role as part of the self-regulatory program supported by the cosmetic industry.

I have had the privilege of being on the CIR Expert Panel for five years, the last two, as Chairman. Each member of the CIR Expert Panel is chosen solely on the basis of her or his individual scientific discipline and expertise. We have no direct financial interest in, or consulting associations with any cosmetic company. Serving with me on the CIR Expert Panel are Wilma F. Bergfeld, M.D. from the Cleveland Clinic Foundation (Medical Specialty: Dermopathology); Roswell K. Boutwelll, Ph.D. from the McArdle Laboratories for Cancer Research, University of Wisconsin (Scientific Specialty: Oncology); William W. Carlton, D.V.M., Ph.D. from Purdue University (Scientific Specialty: Pathology); Dietrick K. Hoffman, Ph.D. from the American Health Foundation (Scientific Specialty: Chemical Carcinogenicity); Arnold L. Schroeter, M.D. from Wright State University, School of Medicine (Medical Specialty: Clinical Dermatology); and Ronald C. Shank, Ph.D. from the University of California (Scientific Specialty: Carcinogenesis/Toxicology). My own particular scientific interests are related to pharmacology/toxicology.

I am aware that the management details, policies and procedures followed by CIR will be reviewed thoroughly by Dr. Elder. The entire CIR administrative program is designed to provide the Expert Panel an environment in which we may work independently and be free of the various other problems faced by the cosmetic industry. The Panel makes judgements on the adequacy of the available safety test data relative to the safety of the numerous chemical ingredients as used in cosmetics. The CIR Procedures limit the Expert Panel to one of three decisions. They are: the ingredients are safe, unsafe, or there are insufficient data to prove safety. To accomplish this demanding task, Panel members make their decisions solely on the basis of the scientific evidence related to safety. Other issues such as market considerations, "popularity" of an ingredient, etc. are never involved in safety decisions.

In the late 1970s there were numerous conferences and discussions on the need for a science court to evaluate the safety of chemicals that might have long-term environmental effects and in that context have a significant impact on the lives of many people. This court would have been set aside from the normal problems and restrictions of an advisorial legal system. I believe that the CIR Program and its Expert Panel, as it was designed and operates, provides such a scientific court for the review of cosmetic ingredients. I know of no other Panel or committee effort that is involved in reviewing chemical ingredient safety that works as openly, or one that encourages the concurrent review of all safety test data by any person or organization during the decision-making process. I believe that these procedural requirements imposed on the Expert Panel makes the CIR Program as close to a true science court as has been achieved outside of the Initial Review Group (study section) system of the National Institutes of Health.

Over the past ten years, the Expert Panel has reviewed and evaluated a wide variety of chemical ingredients used in cosmetics. Many of these chemicals have multiple uses which extend far beyond that of cosmetic product use. Some decisions dealt with controversial ingredients, such as the Expert Panel's decision on formaldehyde. New scientific studies on formaldehyde available since that decision continue to support the Panel's conclusion. I am pleased to call this to your attention and to note that all of the Panel's past decisions have passed equally severe scrutiny. As a scientist, this is the ultimate test of the program's success. However, should new data indicate that a Panel's conclusion is questionable and should be reconsidered, the CIR Expert Panel will not hesitate to re-evaluate an ingredient's safety. Such reconsideration, however, must be based on new and credible scientific data related to safety.

I believe the key to CIR's past success has been due not only to the hard work of the CIR Expert Panel and its staff, but also because it has received the cooperation and support from consumers, government and industry. The representatives from the Consumer Federation of America who have served on the Panel have had a significant impact on the Panel's deliberations and conclusions. The representatives from FDA have contributed immensely to the Panel's understanding of cosmetic ingredient safety. The Expert Panel members have been impressed by the individual members of CTFA who have voluntarily released to CIR, and thus to their competitors, extensive unpublished safety test data. It is impossible to estimate the number of dollars that have been invested by the cosmetic industry in safety test programs that were never published until they were given to CIR. In many instances, specific test procedures were undertaken at the request of the CIR Expert Panel.

The workload of the Expert Panel and its staff has been and continues to be quite heavy. At a recent two-day meeting, sixteen scientific reports, at various stages of development, were reviewed and discussed by panel members. Soon the more frequently used cosmetic ingredients will have been reviewed. The work of CIR will not end, for the Expert Panel has already started its discussions on how the Panel should select less frequently used ingredients for review, knowing all too well that the Panel's review will have a major impact on the use and sale of tke ingredients selected for review. I hope the existing CIR Program, which I prefer to think of as a science court for the review of cosmetic ingredients safety, will continue to serve the consumer and industry as it has been doing for more than ten years.

If I may be of assistance to you or the Committee, please do not hesitate to contact me.

Sincerely,

William O. Berndt, Ph.D.
Vice Chancellor
University of Nebraska
Medical Center

WOB/mar

# COSMETIC INGREDIENT REVIEW

# PROCEDURES

REVISED

Includes amendments approved by CIR Steering Committee and CTFA Board of Directors as of April 26, 1985.

# COSMETIC INGREDIENT REVIEW PROCEDURES

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# COSMETIC INGREDIENT REVIEW

## PROCEDURES

## Part A — General

### Section 1. Definitions.

(a) "Act" means the Federal Food, Drug, and Cosmetic Act.

(b) "Cosmetic" means (1) articles intended to be rubbed, poured, sprinkled, or sprayed on, introduced into, or otherwise applied to the human body or any part thereof for cleansing, beautifying, promoting attractiveness, or altering the appearance, and (2) articles intended for use as a component of any such articles; except that it shall not include soap.

(c) "Cosmetic ingredient" means any chemical substance used as a component in the manufacture of a cosmetic product, but shall not include a proprietary mixture.

(d) "Cosmetic product" means a finished cosmetic the manufacture of which has been completed.

(e) "Commercial distribution" of a cosmetic product means annual gross sales in excess of $1,000 for the product.

(f) "Chemical description" means a concise definition of the chemical composition using standard chemical nomenclature so that the chemical structure or structures of the components of the ingredient would be clear to a practicing chemist. When the composition cannot be described chemically, the substance shall be described in terms of its source and processing.

(g) "Flavor" means any natural or synthetic substance or substances used solely to impart a taste to a cosmetic product.

(h) "Fragrance" means any natural or synthetic substance or substances used solely to impart an odor to a cosmetic product.

(i) "Cosmetic Ingredient Review" means the Cosmetic Ingredient Review program conducted pursuant to these procedures.

(j) "CTFA" means the Cosmetic, Toiletry and Fragrance Association, Inc.

(k) "Director" means the Director of the Cosmetic Ingredient Review, who shall have the authority and responsibilities established in Section 12 of these procedures.

(l) Deleted

(m) "Scientific Coordinator" means the Scientific Coordinator of the Cosmetic Ingredient Review, who shall also be the Executive Secretary of the Expert Panel, who shall have the authority and responsibilities established in Section 14 of these procedures.

(n) "Expert Panel" means the Cosmetic Ingredient Review Expert Panel, which shall be established and shall have the authority and responsibilities established in Part C of these procedures and shall conduct the Cosmetic Ingredient Review program in accordance with the procedures established in Part D of these procedures.

(o) "Executive Secretary" means the Executive Secretary of the Expert Panel, who shall be the Scientific Coordinator and shall have the authority and responsibilities established in Section 14 of these procedures.

(p) "Safe" or "safety" means no evidence in the available information that demonstrates or suggests reasonable grounds to suspect a hazard to the public under the conditions of use that are now current or that might reasonably be expected in the future, e.g., a low incidence of minor adverse reactions (as shown in animal or human testing or product experience). Such information includes, but is not limited to, the chemical structure of the ingredient, published and unpublished tests on the ingredient and products containing the ingredient, significant human experience on products containing the ingredient during marketing, and information on similar or related substances. A lack of information about an ingredient shall not be sufficient to justify a determination of safety.

(q) "Conditions of use" for an ingredient or product include (1) the amount of an ingredient used in a product, (2) the intended and reasonably foreseeable areas of use (e.g., use that is subject to ingestion or inhalation or contact with mucous membranes or is in the area of the eye), and (3) directions for use and against misuse in labeling.

## Section 2. Purpose of the Cosmetic Ingredient Review.

The purpose of the Cosmetic Ingredient Review is to determine those cosmetic ingredients for which there is a reasonable certainty in the judgment of competent scientists that the ingredient is safe under its conditions of use.

## Section 3. Interpretation and Amendment of Procedures.

(a) If any dispute arises as to the proper interpretation or application of these procedures, a majority vote of the Steering Committee shall be final and binding with respect to such matter.

(b) These procedures may be amended by a two-thirds vote of the Steering Committee, with the approval of the CTFA Board of Directors. The Director shall give public notice of any amendment of these procedures.

## Part B — The Cosmetic Ingredient Review Steering Committee and Staff

## Section 10. Organization of the Cosmetic Ingredient Review.

(a) General policy and direction for the Cosmetic Ingredient Review shall be given by a Steering Committee. A quorum of the Steering Committee shall consist of three members. Any matter before the Steering Committee shall be decided by a majority vote of the members present at the time except where otherwise specifically provided in these procedures. The Steering Committee shall consist of the following members:

(1) The President of CTFA, who shall serve as the Chairman of the Steering Committee.

(2) A dermatologist, who shall represent the American Academy of Dermatology.

(3) A toxicologist, who shall represent the Society of Toxicology.

(4) The Chairman of the CTFA Scientific Advisory Committee.

(5) The CTFA Vice President for Science.

(b) The Cosmetic Ingredient Review staff shall consist of a Director, who shall report to the Cosmetic Ingredient Review Steering Committee, and the Scientific Coordinator, who shall report to the Director. The Director and Scientific Coordinator may in turn utilize such other personnel as is necessary and appropriate to carry out their authority and responsibilities established in Sections 12 and 14 of these procedures.

## Section 11. Separation and Independence of the Cosmetic Ingredient Review Staff from the CTFA Staff.

(a) The Cosmetic Ingredient Review staff shall be employees of or consultants to CTFA but shall be separate and independent from the CTFA staff. No person on the Cosmetic Ingredient Review staff may also serve on the CTFA staff. The Cosmetic Ingredient Review staff may obtain supplies and services through the central facilities of CTFA. Contact between the Cosmetic Ingredient Review staff and the CTFA staff shall be kept to the minimum necessary to conduct the affairs of the Cosmetic Ingredient Review efficiently and effectively. CTFA staff shall be treated by the Cosmetic Ingredient Review staff the same as any other member of the public (e.g., all CTFA staff shall sign the visitors log when visiting the Cosmetic Ingredient Review offices).

(b) The Cosmetic Ingredient Review staff shall follow all personnel policies and procedures established in the CTFA Procedures Manual, except that the Director shall be responsible for all required approvals within the authority granted to him under Section 12 of these procedures.

## Section 12. Director.

(a) The Director shall be appointed by the CTFA President, with the approval of the Chairman of the CTFA Board of Directors and the Chairman of the CTFA Scientific Advisory Committee.

(b) The Director shall hire and direct the activities of the Cosmetic Ingredient Review staff in order to implement these procedures effectively and efficiently. The Director shall report to and be subject to the direction and control of the Steering Committee with respect to policy and budget within the following limitations:

(1) The CTFA Board of Directors shall determine the budget and personnel limits for the Cosmetic Ingredient Review.

(2) The Steering Committee shall periodically review all Cosmetic Ingredient Review expenditures (e.g., document reproduction, communications, accounting, and office space expenditures) to determine that they are within the budget.

(3) All Cosmetic Ingredient Review contracts and capital expenditures shall be reviewed and approved by the Steering Committee prior to execution.

(4) All Cosmetic Ingredient Review office supplies shall be obtained through CTFA central purchasing unless otherwise approved by the Steering Committee.

(c) The Scientific Coordinator may simultaneously serve as the Acting Director in the absence of the Director, or as the Director. The Director shall have authority and responsibility for daily administration of the Cosmetic Ingredient Review staff and Expert Panel. This shall include receipt of all documents submitted by any interested person with respect to the Cosmetic Ingredient Review, distribution of all data and information to the Expert Panel, arranging for all aspects of the meetings of the Expert Panel, including public notice thereof, serving as secretary to the Steering Committee, and all similar administrative functions.

Section 13. Deleted

## Section 14. Scientific Coordinator.

The Scientific Coordinator, under the direction of the Director shall have authority and responsibility to perform all of the scientific functions of the Cosmetic Ingredient Review staff (including, but not limited to, the information science function and obtaining all necessary Scientific Literature Reviews) and of the Expert Panel (including, but not limited to, preparing minutes of all meetings, drafting scientific position papers, and otherwise serving as Executive Secretary to the Expert Panel).

## Part C -- The Cosmetic Ingredient Review Expert Panel and Liaison Representatives

## Section 20. Members of the Expert Panel and Liaison Representatives.

(a) Members of the Expert Panel shall possess the following qualifications:

(1) Members shall possess expertise relevant to the review of the safety of cosmetic ingredients. They shall have diverse professional education, training, and experience so that the Expert Panel will reflect a balanced composition of sufficient scientific expertise to handle the issues that come before it.

(2) Members shall be required to meet the same conflict of interest standards as are applicable under Federal Law to special government employees.

(3) Liaison representatives shall be selected by the interested organizations as provided in Section 22 of these procedures. Technical expertise with the subject matter with which the Expert Panel is involved shall not be a requirement.

(b) Members appointed to the Expert Panel and liaison representatives shall continue to serve for the duration of the Expert Panel or until they resign or are removed from membership for cause by the Steering Committee.

(c) An Expert Panel member may be removed from membership by the Steering Committee for good cause. Good cause shall include but not be limited to excessive absenteeism from Expert Panel meetings, a demonstrated bias which interferes with the ability to render objective advise, or failure to abide by these procedures.

(d) There shall ordinarily be seven members of the Expert Panel, each member having an equal vote. The Expert Panel shall begin to function, and may continue to function, as long as there are not less than five members.

## Section 21. Nominations and Selection of Members of the Expert Panel.

(a) The Director shall give public notice requesting nominations for members of the Expert Panel. The notice shall invite the submission of —

nominations for members from any interested individual as well as from consumer, industry, and professional organizations, within 90 days of such notice.

(b) Any interested person may nominate one or more qualified person(s) as a member of the Expert Panel. Nominations shall include a complete curriculum vitae of the nominee, and shall state that the nominee is aware of the nomination, is willing to serve as a member of the Expert Panel, and appears to have no conflict of interest which would preclude membership on the Expert Panel.

(c) Members of the Expert Panel shall serve as individuals and not as representatives of any group or organization which nominated them or with which they may be affiliated.

(d) The Steering Committee shall appoint the members of the Expert Panel from among those who have been nominated. Appointment shall be decided by a four-fifths vote of all current members of the Steering Committee. Appointment shall be on the basis of scientific competence, expertise in an area relevant to the Cosmetic Ingredient Review, balance of scientific disciplines within the Expert Panel, willingness to devote sufficient time and energy to the review, and the lack of any disqualifying conflict of interest.

(e) All data and information relating to the nomination and selection of the members of the Expert Panel shall be maintained by the Director in a confidential file.

(f) Vacancies in the membership of the Expert Panel shall be filled by the Steering Committee either from prior nominations or in the same way that members are initially nominated and selected.

## Section 22. Selection of Liaison Representatives to the Expert Panel.

(a) The Director shall request that each of the following interests designate a liaison representative to the Expert Panel:

(1) The Food and Drug Administration, in accordance with the provisions of proposed 21 C.F.R. 2.21(d).

(2) Organizations representing consumer interests.

(3) CTFA.

(b) Liaison representatives to the Expert Panel shall be limited to three persons, one representing each of the listed interests. Those interests may, however, designate different liaison representatives for purposes of the review of different categories of cosmetic ingredients or similar considerations. At no time may there be more than one liaison representative to the Expert Panel from any one of the interests listed in Section 22(a) of these procedures with respect to any specific cosmetic ingredient.

(c) Because liaison representatives for government, consumer, and industry interests have no vote, their selection shall be solely by the interests they represent and shall be without regard to the conflict of interest principles for special government employees that are applicable to the members of the Expert Panel.

(d) Vacancies in the liaison representatives to the Expert Panel shall be filled in the same way that liaison representatives are initially selected.

## Section 23. Rights and Responsibilities of Liaison Representatives to the Expert Panel.

(a) A liaison representative to the Expert Panel selected to represent and serve as a liaison with interested individuals, associations, and organizations, shall have the same rights as members of the Expert Panel except that:

(1) A liaison representative shall not vote on any matter before the Expert Panel.

(2) A liaison representative shall not have access to confidential data and information that are not available for public disclosure pursuant to Section 51(b) of these procedures. Accordingly, a liaison representative shall not be present at any portion of an Expert Panel meeting which is closed for the presentation of confidential data pursuant to Section 34(c) or the discussion of confidential data pursuant to Sections 34(d) and 36(b)(2) of these procedures which are prohibited from public disclosure pursuant to Section 51(b) of these procedures.

(b) A liaison representative of the Expert Panel is subject to, and shall abide by, all aspects of these procedures and any rules and regulations adopted by the Expert Panel pursuant to Section 32 of these procedures.

(c) It is the responsibility of the liaison representatives to the Expert Panel to represent the government, consumer, and industry interests in all deliberations.

(1) The consumer and industry liaison representative does not represent any particular organization or group, but rather represents all interested persons within the class which he is selected to represent. Accordingly, any interested person within the class represented by that liaison representative shall have access to all written statements or oral briefings related to the Expert Panel prepared by the liaison representative for distribution to any person outside the Expert Panel.

(2) Liaison representatives shall review all official Expert Panel minutes to assure their completeness and accuracy.

(3) The liaison representative shall act as a liaison with and conduits between the Expert Panel and the interested persons whom he represents, and shall transmit requests for information from the Expert Panel and relevant data, information, and views to the Expert Panel. He shall take the initiative in contacting interested persons whom he represents, to seek out relevant data, information, and views, and to relate the progress of the Expert Panel.

(4) The industry liaison representative shall represent all members of the industry, and not any particular association, company, product, or ingredient. If a matter comes before the Expert Panel that directly or indirectly affects the company which employs the industry liaison representative, he need not absent himself during the discussion or decline to participate in the discussion. The industry liaison representative shall not discuss his company's position as such, but may discuss any matter in general terms. All presentations and discussions of scientific data and their interpretation on behalf of a company shall occur in open session, except as provided in Section 34(c) of these procedures.

(5) A liaison representative to the Expert Panel shall not make any presentation to the Expert Panel during a hearing conducted by the Expert Panel.

(6) Although a liaison representative is serving in a representative capacity, he shall exercise restraint in performing his functions and shall not engage in unseemly advocacy or attempt to exert undue influence over members of the Expert Panel.

(c) A liaison representative to the Expert Panel may be removed by the Steering Committee for failure to comply with the provisions of this section or the other sections of these procedures. In the event of removal of a liaison representative, the interests which he has represented shall be requested to select a new liaison representative.

## Section 24. Compensation of Expert Panel Members.

(a) All members of the Expert Panel and liaison representatives shall receive a consultant fee and be reimbursed for their travel expenses and all other out-of-pocket expenses, unless such compensation and reimbursement is waived.

(b) An Expert Panel member or liaison representative notwithstanding his primary residence, while in attendance at meetings of the Expert Panel, will be paid whether the meetings are held in his city of residence or elsewhere.

(c) An Expert Panel member or liaison representative who participates in a specific assignment for the Expert Panel, at the request of the Cosmetic Ingredient Review, will be paid at an hourly rate when he performs his work at home, place of business, or elsewhere, and at a daily rate when he is required to travel outside of his commuting area to perform his assignment. An Expert Panel member or liaison representative will not be paid for time spent on normal preparation for a meeting of the Expert Panel.

(d) Salary while in travel status is authorized when an Expert Panel member or liaison representative has his ordinary pursuits interrupted for the substantial portion of an additional day beyond the day or days on which he performs services, and as a consequence he sustains a loss in his regular compensation. This applies on weekends and holidays if the Expert Panel member or liaison representative suffers a loss in income he would otherwise earn on that day. For travel purposes, a substantial portion of a day is defined as 50 percent of the working day, and the traveller will be paid at a daily rate.

## Section 25. Chairman of the Expert Panel.

(a) The Steering Committee shall select the Chairman of the Expert Panel from among the members, who may serve on a permanent or on a rotating basis.

(b) The Expert Panel Chairman shall have the authority to conduct hearings and meetings, including the authority to adjourn any hearing or meeting whenever he determines adjournment to be advisable, to discontinue discussion of a particular matter, to conclude the open portion of a meeting in accordance with Section 36 of these procedures, or to take any other action in furtherance of a fair and expeditious hearing or meeting.

## Section 26. Ex Parte Contacts With the Expert Panel.

(a) There shall be no ex parte contacts between the members of the Expert Panel and anyone other than a liaison representative to the Expert Panel or a member of the Cosmetic Ingredient Review staff with respect to any matter relating to the Cosmetic Ingredient Review, except that:

(1) The Steering Committee may meet with the Expert Panel or any members thereof or any liaison representatives to discuss the work of the Expert Panel.

(2) A member of the Expert Panel may, in his discretion, initiate discussions with any other scientist for the purpose of obtaining data, information, or views with respect to any scientific issue.

(b) If any person initiates an ex parte contact with a member of the Expert Panel other than as permitted by paragraph (a) of this section, such member shall refer such person to the Cosmetic Ingredient Review staff for advice on the procedures for submission of data, information, and views to the Expert Panel.

### Section 27. Compilation of Background Materials for Members of the Expert Panel and Liaison Representatives.

The Director shall prepare and provide to Expert Panel members and liaison representatives a complete compilation of background materials bearing upon their duties and responsibilities.

## Part D — The Cosmetic Ingredient Review Procedures

### Section 30. Compilation of Safety Data and Information and Review by the Expert Panel.

(a) The Steering Committee shall develop a tentative priority list(s) for the systematic review of all cosmetic ingredients presently used in commercially distributed cosmetic products. This tentative priority list(s) shall be based upon the frequency of use (*i.e.,* the number of different products in which an ingredient is used), availability of chemical specifications or descriptions, any known questions about safety, and the availability of sufficient data and information for the Expert Panel to make an informed scientific judgment on safety.

(1) For those cosmetic ingredients for which no particular priority can be established, their priority shall be determined by a statistically reliable randomization.

(2) For those cosmetic ingredients which are also subject to other existing safety reviews, their inclusion and priority shall be determined pursuant to paragraph (i) of this section.

(b) The tentative priority list(s) shall be made publicly available and 90 days will be provided for public comment on it.

(c) The Expert Panel shall review the tentative priority list(s) and all comments received on it, make any revisions it concludes appropriate, and adopt a final priority list(s). The final priority list(s) shall determine the order in which cosmetic ingredients are reviewed under the Cosmetic Ingredient Review. The Expert Panel may at any time revise the final priority list(s) either to add new ingredients or to revise the priority of existing ingredients.

(d) On the basis of the tentative and final priority list(s) the Scientific Coordinator shall develop or obtain Scientific Literature Reviews for each cosmetic ingredient (or, where appropriate, closely related groups of cosmetic ingredients), which shall consist of a bibliography of the domestic and foreign toxicological literature and any other major domestic and foreign scientific literature, a description of each literature reference, and a summary of the information found for each ingredient.

(1) The Scientific Coordinator may either contract for the preparation of each Scientific Literature Review or prepare it himself.

(2) As soon as it is available, each Scientific Literature Review will be made public and 90 days will be provided for public comment on it.

(3) If the Scientific Coordinator concludes that there is insufficient scientific literature to justify the preparation of a Scientific Literature Review, the Director shall give public notice that no Scientific Literature Review will be prepared for the ingredient involved.

(e) Upon the public notice of the availability of a Scientific Literature Review, or that no Scientific Literature Review will be prepared, all interested persons will be provided 90 days to submit to the Director data, information, and views relevant to the safety of the cosmetic ingredient involved. A person may submit any particular piece of information without identifying the source of that information. To be considered, twelve copies of the data and views shall be submitted, preferably bound, indexed, and on standard size paper (approximately 8 1/2 by 11 inches). All submissions shall be in the following format:

## COSMETIC INGREDIENT REVIEW INFORMATION

I. The CTFA adopted name(s) and tradename(s) of the cosmetic ingredient(s) involved, the name of the manufacturer, and if it does not meet the specifications in any of the information sources designated in the CTFA Cosmetic Ingredient Dictionary a statement to that effect and the specifications that are applicable.

II. Comments, if any, on the completeness and accuracy of the Scientific Literature Review for the ingredient.

III. A statement setting forth the number of products containing the ingredient manufactured or distributed by the person making the submission, and the pertinent letter for each indicating the range of the concentration of the ingredient for each product, as is shown in the information submitted to the Food and Drug Administration on Form FD-2512 (Cosmetic Product Ingredient Statement), 21 C.F.R. 720.4(d) (1).

IV. Animal safety data.

A. All animal safety data not included in the Scientific Literature Review on the individual cosmetic ingredient.

B. All animal safety data not included in the Scientific Literature Review on combinations of the individual cosmetic ingredient.

C. All animal safety data not included in the Scientific Literature Review on cosmetic products or other products containing the individual cosmetic ingredient as one component.

V. Human safety data (including exposure during clinical testing, in occupational settings, and through product use).

A. All human safety data not included in the Scientific Literature Review on the individual cosmetic ingredient.

B. All human safety data not included in the Scientific Literature Review on combinations of the individual cosmetic ingredients.

C. All human safety data not contained in the Scientific Literature Review on cosmetic products or other products containing the individual cosmetic ingredient as one component, including results of significant human experience during marketing. Such data may include relevant Form FD-2704 (Cosmetic Product Experience Report), FD-2705 (Cosmetic Product Unusual Experience Report), and FD-2706 (Summary Report of Cosmetic Product Experience by Product Categories), 21 C.F.R. Part 730.

VI. Other Relevant Safety Information.

VII. Conditions of use.

A. A statement that the ingredient is or is not used in a cosmetic which falls into the following general use classifications.

1. Eye area use.
2. Subject to incidental ingestion.
3. Subject to incidental inhalation.
4. Mucous membrane use.
5. All other uses (e.g., skin, hair, and nails).

B. A statement indicating the use classifications for each of the products in which the ingredient is used by the manufacturer or distributor, as specified in Food and Drug Administration Form FD-2512 (Cosmetic Product Ingredient Statement), 21 C.F.R. 720.4(c).

C. Information on any other relevant conditions of use (e.g., directions for use and against misuse).

VIII. A summary of the data and views setting forth the rationale for the conclusion that the ingredient is or is not safe for its intended use.

(f) Upon the public notice of the availability of a Scientific Literature Review, CTFA and any other interested person may submit to the Director a chemical description of the ingredient involved, if one is available.

(g) Upon expiration of the time permitted for receipt of all of the pertinent data and information, the Scientific Coordinator shall prepare a final compilation of relevant data and information for presentation to the Expert Panel. That compilation shall include:

(1) The Scientific Literature Review.

(2) All comments received on the Scientific Literature Review.

(3) All submissions of data and information not contained in the Scientific Literature Review.

(4) All chemical descriptions submitted.

(h) The Expert Panel may, in its discretion, accept late submissions and new data relating to any ingredient at any time prior to its tentative report on that ingredient.

(i) To minimize duplication of effort, the inclusion and priority of cosmetic ingredients which are also subject to other existing safety reviews shall be determined as follows, except that any specific ingredient the review of which would otherwise be deferred shall nonetheless be included at the discretion of the Expert Panel when other chemically related or otherwise conveniently grouped ingredients are considered, and except with respect to any specific ingredient for which the Expert Panel has assigned a special priority for good cause with the approval of the Steering Committee.

(1) Color Additives. All color additives shall be excluded from the Cosmetic Ingredient Review because their safety is determined under Section 706 of the Act and 21 C.F.R. Parts 8 and 9.

(2) OTC Drug Active Ingredients. The Expert Panel shall defer evaluation of a cosmetic ingredient which is also used as an active ingredient in an OTC drug, and thus is subject to review under the Food and Drug Administration OTC drug review established in 21 C.F.R. Part 330, until after the final monograph for the relevant OTC drug category (or, if there is more than one, the last relevant OTC drug category) is published by the Food and Drug Administration pursuant to 21 C.F.R. 330.10(a)(9) and shall then

determine whether all safety information relevant to cosmetic use of the ingredient was available to the OTC drug review and whether the cosmetic use of the ingredient presents any additional safety considerations not adequately covered by the OTC drug review. The Expert Panel shall adopt those conclusions of the OTC drug review which it concludes adequately cover cosmetic use of the ingredient and shall conduct its own evaluation of those cosmetic uses not adequately covered by the OTC drug review.

(3) Food Flavors. The Expert Panel shall defer evaluation of a cosmetic flavor ingredient which is also used as a flavor in food, and thus is subject to review under the FASEB-FDA review of flavor ingredients which are GRAS or food additives described in Part II of the Federal Register of July 26, 1973 (38 F.R. 20036 et seq.) and Part II of the Federal Register of September 23, 1974 (39 F.R. 34172 et seq.), until after the final regulation for the ingredient is published by the Food and Drug Administration and shall then determine whether all safety information relevant to cosmetic use of the ingredient was available to the FASEB-FDA review and whether the cosmetic use of the ingredient presents any additional safety considerations not adequately covered by the FASEB-FDA review. The Expert Panel shall adopt those conclusions of the FASEB-FDA review which it concludes adequately cover cosmetic use of the ingredient and shall conduct its own evaluation of those cosmetic uses not adequately covered by the FASEB-FDA review.

(4) GRAS Food Ingredients. The Expert Panel shall defer evaluation of a cosmetic ingredient which is also used as an ingredient in a food on the basis that it has been determined to be GRAS or subject to a prior sanction,

and thus is subject to review under the FASEB-FDA review described in Part II of the Federal Register for July 26, 1973 (38 F.R. 20036 et seq.) and Part II of the Federal Register for September 23, 1974 (39 F.R. 34172 et seq.), until after the final regulation is promulgated for the ingredient by the Food and Drug Administration and shall then determine whether all safety information relevant to cosmetic use of the ingredient was available to the FASEB-FDA review and whether the cosmetic use of the ingredient presents any additional safety considerations not adequately covered by the FASEB-FDA review. The Expert Panel shall adopt those conclusions of the FASEB-FDA review which it concludes adequately cover cosmetic use of the ingredient and shall conduct its own evaluation of those cosmetic uses not adequately covered by FASEB-FDA review.

(5) Food Additives. In evaluating a cosmetic ingredient which is also used as a food additive, and thus is subject to a food additive regulation promulgated by the Food and Drug Administration in 21 C.F.R. Part 121, the Expert Panel shall review the food additive petition and all related documents which the Food and Drug Administration makes available to determine whether all safety information relevant to cosmetic use of the ingredient was available to the Food and Drug Administration and whether the cosmetic use of the ingredient presents any additional safety considerations not adequately covered by the Food and Drug Administration approval of the food additive regulation. The Expert Panel shall adopt those conclusions of the Food and Drug Administration approval which it concludes adequately cover cosmetic use of the ingredient and shall conduct its own evaluation of those cosmetic uses not adequately covered by the Food and Drug Administration approval.

(6) Fragrance Ingredients. All fragrance ingredients shall be excluded from the Cosmetic Ingredient Review because their safety is being determined by the Research Institute for Fragrance Materials (RIFM).

(7) Food and Drug Administration Regulations. All matters which are the subject of a final regulation promulgated by the Food and Drug Administration shall be excluded from the Cosmetic Ingredient Review.

(8) New Drug Applications. In evaluating a cosmetic ingredient which is also used as an inactive or active ingredient in an OTC or prescription drug for which the Food and Drug Administration has at any time approved or permitted to become effective a New Drug Application, the Expert Panel shall review all related documents which the Food and Drug Administration makes available to determine whether all safety information relevant to cosmetic use of the ingredient was available to the Food and Drug Administration and whether the cosmetic use of the ingredient presents any additional safety considerations not adequately covered by the Food and Drug Administration action on the New Drug Application. The Expert Panel shall adopt those conclusions of the Food and Drug Administration action which it concludes adequately cover cosmetic use of the ingredient and shall conduct its own evaluation of those cosmetic uses not adequately covered by the Food and Drug Administration action.

(j) An ingredient shall be reviewed in accordance with the priority assigned to it pursuant to this section.

(1) Upon presentation of all pertinent data and information to the Expert Panel pursuant to paragraph (g) of this section, an ingredient shall be considered to be under review by the Expert Panel. An ingredient shall remain under review by the Expert Panel until the Expert Panel issues a final report on it pursuant to Section 45 of these procedures.

(2) If the Expert Panel concludes that the available data and information are insufficient to determine such ingredient, under each relevant condition of use, as either safe or not safe, it shall decide the type of further data or information required and the time period within which it might reasonably be obtained. Any such decision shall be set forth fully in the minutes of the Expert Panel meeting.

(A) Upon the public availability of the minutes of any such meeting pursuant to Section 51 of these procedures, the Director shall give public notice of any such decision.

(B) Within 90 days after such public notice, any interested person may inform the Expert Panel that work adequate and appropriate to resolve the questions raised about the ingredient will be undertaken.

(C) A progress report on any work undertaken pursuant to such a commitment shall be filed with the Cosmetic Ingredient Review every January 1 and July 1 until completion.

(D) If such a commitment is undertaken, the ingredient shall remain under review by the Expert Panel and the Expert Panel shall defer preparation of a tentative report pursuant to Section 44 of these procedures and a final report pursuant to Section 45 of these procedures until completion of the work involved, unless the Expert Panel determines that the work is not being pursued promptly and diligently or that interim results indicate a reasonable likelihood that a health hazard exists.

(E) Upon completion of the work undertaken pursuant to such a commitment, the Expert Panel shall review all available data and information and shall issue a tentative report pursuant to Section 44 of these procedures and a final report pursuant to Section 45 of these procedures.

(3) If the Expert Panel determines pursuant to paragraph (j) (2) of this section that the available data and information are insufficient to determine such ingredient, under any specific condition of use, as either safe or not safe, and no one undertakes the work to obtain the required data and information in accordance with paragraph (j) (2) of this section, the Expert Panel shall determine that there is a lack of information needed to make a determination and insufficient industry interest in the ingredient at that time to justify obtaining the needed information and shall issue a tentative report pursuant to Section 44 of these procedures and a final report pursuant to Section 45 of these procedures.

## Section 31. Meetings of the Expert Panel.

(a) The Expert Panel will meet as often and for as long as is appropriate to review the data submitted to it and to prepare a report containing its conclusions and recommendations with respect to the safety of cosmetic ingredients.

(b) The Expert Panel shall convene at the call of the Chairman. The Director shall be responsible for giving appropriate notice to all Expert Panel members and liaison representatives for distributing all pertinent information, for all travel and meeting arrangements, and for similar administrative support.

(c) All Expert Panel meetings shall be held in Washington, D.C., or the immediate vicinity, unless there are compelling reasons for a different location. A different location may be approved by the Steering Committee for good cause.

(d) The Expert Panel may, with the approval of the Steering Committee, conduct on-site visits relevant to the work of the Expert Panel.

(e) A quorum for the Expert Panel shall be five members of the Expert Panel. Any matter before the Expert Panel shall be decided by a majority vote of the members present at the time, except that any final report shall be voted upon by all current members of the Expert Panel. Any current member of the Expert Panel may file a separate report with additional or minority views.

(f) Subject to availability of space, any interested person may attend any portion of any Expert Panel meeting which is not closed.

(g) Any portion of a meeting shall be closed by the Expert Panel Chairman when matters which have been determined closed in accordance with Section 36 of these procedures are to be discussed. Where a portion of the meeting is closed, the closed portion shall be held after the conclusion of the open portion whenever practicable.

(h) Any Expert Panel member or liaison representative may take notes during Expert Panel meetings and report and discuss the deliberations of the Expert Panel after a meeting is completed and before official minutes or a report is available, within such rules and regulations as are adopted by the Expert Panel in accordance with Section 32 of these procedures.

(1) There shall be no attribution of individual views expressed in a closed session or revealing of numerical votes.

(2) There shall be no reporting or discussion with respect to any particular matter where the Expert Panel specifically so directs, e.g., where deliberations are incomplete or involve a sensitive decision which should not be released prematurely.

(3) There shall be no reporting or disclosure with respect to data or information prohibited from public disclosure pursuant to Section 51(b) of these procedures.

(4) Any notes or minutes kept or report prepared by any Expert Panel member or liaison representative shall have no status or effect whatever

unless adopted as or incorporated into the official minutes or report by the Expert Panel. It shall be the responsibility of each Expert Panel member and liaison representative to make certain that the official minutes and reports are complete and accurate and fully reflect what happened at any meeting he attended.

## Section 32. Additional Rules for the Expert Panel.

(a) In addition to the rules established in these procedures, the Expert Panel may, with the concurrence of the Steering Committee, adopt additional rules which are not inconsistent with these procedures.

(b) Such additional rules shall be included in the minutes of the meeting when adopted and in the materials compiled pursuant to Section 27 of these procedures and shall be available for public disclosure pursuant to Section 51(a) of these procedures.

## Section 33. Consultation by the Expert Panel with Other Persons.

(a) The Expert Panel may consult with any person who may have data, information, or views relevant to any matter pending before the Expert Panel and, with the approval of the Director and the Chairman of the Steering Committee, may compensate such person and reimburse his expenses.

(b) Any interested person may submit to the Expert Panel a written request that it consult with specific persons who may have data, information, or views relevant to any matter pending before the Expert Panel. Such requests shall state why the specified person should be consulted and, if payment is requested, why the views of that person cannot reasonably be furnished to the Expert Panel by any other means. The Expert Panel, may, in its discretion deny or grant such a request and, if payment is requested, with the approval of the Director and the Chairman of the Steering Committee, may compensate such person and reimburse his expenses.

## Section 34. Portions of Expert Panel Meetings.

An Expert Panel meeting shall have the following separable portions:

(a) The open public hearing. Every Expert Panel meeting shall include an open portion which shall constitute a public hearing during which any interested person may present data, information, or views, orally or in writing, relevant to the Expert Panel's agenda or other work. Such hearing shall be conducted in accordance with Section 39 of these procedures.

(b) The open panel discussion. The Expert Panel shall discuss any matter pending before it in an open portion of its meeting unless the meeting has been closed with respect to that matter pursuant to Section 36 of these procedures. No public participation is permissible during the open panel discussion portion of the meeting except with the consent of the Chairman of the Expert Panel.

(c) The closed presentation of data. Data and information which are prohibited from public disclosure pursuant to the provisions of Section 51(b) of these procedures shall be presented to the members of the Expert Panel in a closed portion of its meeting.

(d) The closed panel deliberations. Deliberations with respect to matters pending before the Expert Panel may be made in a closed portion of its meeting upon an appropriate determination by the Chairman pursuant to Section 36 of these procedures.

## Section 35. Notice of Public Hearing and Meeting of the Expert Panel.

(a) At least fifteen days before any meeting of the Expert Panel, the Director shall give public notice of such meeting.

(b) Such notice shall include:

(1) The date, time, and place of the hearing and meeting.

(2) A list of all agenda items.

(3) If any portion of the meeting is closed, a statement of the time of the open and closed portions.

(4) The time specifically set aside for oral statements by interested persons and for other public participation.

(5) The name, address, and telephone number of the persons specifically responsible for the administrative support for that hearing and meeting.

(6) A statement that written submissions may be made to the Expert Panel at any time pursuant to Section 38 of these procedures.

## Section 36. Determination to Close Portions of Expert Panel Meetings.

(a) No Expert Panel meeting shall be entirely closed unless no one requests an opportunity to make a presentation at the open portion for public participation. A portion of an Expert Panel meeting may be closed only pursuant to a determination by the Chairman, reflected in the minutes of the meeting, in accordance with this section.

(b) The following rules shall govern the closing of a portion of an Expert Panel meeting:

(1) Any determination to close a portion of a meeting shall restrict such closing to the shortest time possible consistent with the policy established in this section.

(2) Portions of meetings during which matters are considered that are prohibited from public disclosure pursuant to Section 51(b) of these procedures shall be closed.

(3) Portions of meetings during which the Expert Panel deliberates on the safety of cosmetic ingredients may be closed upon the determination of the Chairman that it is essential to close such portion of such meeting to protect the free exchange of internal views and to avoid undue interference with Expert Panel operations.

(c) A matter which is properly considered in an open portion of an Expert Panel meeting may instead be considered in a closed portion only if it is so inextricably intertwined with matters to be discussed in a closed portion that it is not feasible to separate them or discussion of the matter in an open portion would compromise or impinge upon the matters to be discussed in the closed portion.

(d) A closed portion of an Expert Panel meeting shall be attended only by Expert Panel members, liaison representatives, and the Cosmetic Ingredient Review employees, except as provided in Section 34(c) of these procedures for presentation of data and information which are prohibited from public disclosure pursuant to Section 51(b) of these procedures. Any person making a presentation described in Section 34(c) may be accompanied by a reasonable number of employees, consultants, or other persons with whom he has a commercial arrangement. If any person other than an Expert Panel member, a liaison representative, a Cosmetic Ingredient Review employee, or a person making a presentation described in Section 34(c) attends a portion of an Expert Panel meeting, that portion shall be open to attendance by any interested person.

## Section 37. Administrative Remedies.

Any person who alleges non-compliance by the Expert Panel or the Cosmetic Ingredient Review staff with any provision of these procedures may request appropriate relief from the Steering Committee.

## Section 38. Written submissions to the Expert Panel.

(a) Twelve copies of all written submissions for the Expert Panel shall be sent to the Director, unless an applicable public notice specifies otherwise.

(b) At the request of the Expert Panel, the Director may at any time issue a public notice requesting the submission to the Expert Panel of written data, information, and views pertaining to any matter being reviewed by the Expert Panel. Such notice shall specify the format in which the submission shall be made, the number of copies to be submitted, and the time within which submission shall be made.

(c) Any interested person may submit to the Expert Panel, through the Director, written data, information, or views on any matter being reviewed by the Expert Panel. Voluminous data shall be accompanied by a summary.

(1) Any such submission shall be distributed to each Expert Panel member and liaison representative, either by mail or at the next Expert Panel meeting, and shall be considered by the Expert Panel in its review of the matter.

(2) The Expert Panel may establish, and shall give public notice of, a cut-off date after which submissions relating to any matter shall no longer be received or considered.

(d) The Scientific Coordinator, shall provide for the Expert Panel and liaison representatives all scientific data and information he concludes to be relevant to any matter being reviewed by the Expert Panel. Any member of the Expert Panel or liaison representative shall, upon request, also be provided any additional material available to the Cosmetic Ingredient Review which he believes appropriate for an independent judgment on the matter, e.g., raw data underlying any summary or report.

## Section 39. Conduct of a Public Hearing Before the Expert Panel.

(a) For each Expert Panel meeting, the open portion for public participation which constitutes a public hearing pursuant to Section 34(a) of these procedures shall be at least one hour long unless the public participation does not last that long, and may last for whatever time the Expert Panel Chairman determines will facilitate the work of the Expert Panel. The public notice issued pursuant to Section 35 of these procedures shall designate the time specifically reserved for such public hearing, which shall ordinarily be the first portion of the meeting. Further public participation in any open portion of the meeting pursuant to Section 34(b) of these procedures shall be solely at the discretion of the Expert Panel Chairman.

(b) Any interested person who wishes to be assured of the right to make an oral presentation at a particular Expert Panel hearing shall so inform the Director, orally or in writing, prior to the Expert Panel meeting.

(1) Such person shall state the general nature of the presentation and the approximate time requested. Whenever possible, all written data and information to be discussed by that person at the Expert Panel hearing shall be furnished in advance to the Director or other designated Cosmetic Ingredient Review employee. Such written material shall be mailed to the Expert Panel members and liaison representatives in advance of the meeting if time permits, and otherwise will be distributed to the Expert Panel members and liaison representatives when they arrive at the meeting. Such mailing or distribution shall be undertaken only by the Cosmetic Ingredient Review staff unless the Director specifically permits the person making the presentation to mail or distribute such material.

(2) Prior to the Expert Panel hearing, the Director shall determine the amount of time allocated to each person for his oral presentation and the time that oral presentation is scheduled to begin. Each person shall be so informed in writing or, if the time prior to the hearing is short, by telephone. Joint presentations may be required by persons with common interests.

(c) The Chairman of the Expert Panel shall preside at the hearing and shall be accompanied by other Expert Panel members and liaison representatives who shall serve as a panel in conducting the hearing.

(d) Each person may use his allotted time in whatever way he wishes, consistent with a reasonable and orderly hearing. A person may be accompanied by any number of additional persons, and may present any written data, information, or views for the consideration of the Expert Panel.

(e) If a person is not present at the time specified for his presentation, the persons following will appear in order. An attempt will be made to hear any such person at the conclusion of the hearing. Any interested persons attending the hearing who did not request an opportunity to make an oral presentation shall be given an opportunity to make an oral presentation at the conclusion of the hearing, in the discretion of the Chairman, to the extent that time permits.

(f) The Chairman, other members of the Expert Panel, and liaison representatives may question any person during or at the conclusion of his presentation. No other person attending the hearing may question a person making a presentation. The Chairman may allot additional time to any person when he concludes that it is justifiable, but may not reduce the time allotted for any person without his consent.

(g) Public participants may question an Expert Panel member or a liaison representative only with that person's permission and only about matters before the Expert Panel.

(h) The hearing shall be informal in nature, and the rules of evidence shall not apply. No motions or objections relating to the admissibility of data, information, and views shall be made or considered, but other participants may comment upon or rebut all such data, information, and views. No participants may interrupt the presentation of another participant at any hearing for any reason.

Section 40. Minutes and Reports of Expert Panel Meetings.

(a) The Executive Secretary or other designated Cosmetic Ingredient Review employee shall prepare detailed minutes of all Expert Panel meetings, except that less detailed minutes may be prepared for open portions of meetings which are transcribed or recorded. The accuracy of all minutes shall be approved by the Expert Panel and certified by the Expert Panel Chairman. Such approval and certification may be accomplished by mail and by telephone.

(b) The minutes shall include:

(1) The time and place of the meeting.

(2) The names of the Expert Panel members, the Cosmetic Ingredient Review staff, and the liaison representatives as well as the names and affiliations or interests of public participants attending the meeting.

(3) A copy of or reference to all written information made available for consideration by the Expert Panel at the meeting.

(4) A complete and accurate description of matters discussed and

conclusions reached. Such description shall be kept separately for the following portions of the meeting to facilitate their public disclosure: the open portion specified in Section 34(a) and (b), any closed portion during which a presentation is made pursuant to Section 34(c), and any closed deliberative portion pursuant to Section 34(d). The minutes of a closed deliberative portion of a meeting shall not refer to Expert Panel members by name, except upon their request, or to data or information prohibited from public disclosure under Section 51(b) of these procedures. Any such inadvertent references which do not occur shall be deleted prior to public disclosure.

(5) A copy of or reference to all reports received, issued, or approved by the Expert Panel.

(6) The extent to which the meeting is open and closed to the public.

(7) The extent to public participation, including a list of members of the public who presented oral or written statements.

## Section 41. Transcripts of Expert Panel Meetings.

(a) A transcript or recording is not required for any portion of an Expert Panel meeting.

(b) The Expert Panel shall decide whether any portion or all of its meetings shall be transcribed or recorded and, if so, by what means. Any such transcription or recording shall be arranged by the DIrector.

(c) If a transcript or recording of an open portion of an Expert Panel meeting is made by the Cosmetic Ingredient Review staff, or is made by an interested person and is submitted to the Cosmetic Ingredient Review, it shall be included in the record of the Expert Panel proceedings.

(d) If a transcript or recording of any closed portion of an Expert Panel meeting is made, it shall not be included in the records of the Expert Panel proceedings that are available for public disclosure. Any such transcript or recording shall be retained as confidential. The Chairman of the Expert Panel may, in his discretion, permit discussion without transcription or recording during any closed portion of an Expert Panel meeting that is otherwise being transcribed or recorded.

(e) Any person attending any open portion of an Expert Panel meeting may, consistent with the orderly conduct of the meeting, record or otherwise take his own transcript of the meeting. No person attending any closed portion of any Expert Panel meeting may record or otherwise take his own transcript of the meeting, except for an official transcript or recording arranged by the Director.

## Section 42. Expert Panel Determinations.

On the basis of all data and information submitted to it, the Expert Panel shall determine whether each ingredient, under each relevant condition of use, is safe, or not safe, or there is a lack of information needed to make a determination and insufficient industry interest in the ingredient at that time to justify obtaining the needed information. Upon making such a determination, the Expert Panel shall issue a tentative report pursuant to Section 44 of these procedures and a final report pursuant to Section 45 of these procedures.

## Section 43. Working Teams of Expert Panel Members.

Working teams of Expert Panel members may be designated to review information, to prepare draft documents, or to undertake other specific assignments for the Expert Panel, subject to the following conditions:

(a) The Chairman of the Expert Panel may appoint working teams comprised of from two to four members of the Expert Panel (one of whom may be the Chairman of the Expert Panel) to review information about designated ingredients, to prepare draft documents for consideration by the entire Panel, or to perform other specific assignments for the Expert Panel. The Chairman of the Expert Panel shall assign a leader for each working team.

(b) A meeting of a working team is not a meeting of the Expert Panel and shall be governed by the procedures established by this Section and not by the procedures applicable to meetings of the Expert Panel.

(c) A working team shall meet at the call of its leader, issued through the Director. A working team may meet in Washington, D.C., or at another location if that location is more convenient for the working team members and conserves the resources of the Cosmetic Ingredient Review. Liaison representatives shall be advised of all working team meetings and may attend and participate. Only Expert Panel members, liaison representatives, and CIR staff may attend working team meetings, except upon the specific approval of the Chairman of the Expert Panel, the Director, and the Chairman of the Steering Committee.

(d) Any document distributed by a working team member to other members of the team, including a call for meeting issued by the team leader, shall be distributed through the Director, who shall also simultaneously send the document to the liaison representatives. The Director shall maintain a log and copies of all such documents.

(e) A working team may be assisted by the CIR staff, through the Director.

(f) A document prepared by a working team may be submitted to the Expert Panel by the leader of the working team, through the Director. The Director shall promptly distribute the document to Expert Panel members and to liaison representatives. Such a document should be received by Panel members and liaison representatives at least two weeks before the Panel meeting at which it is to be voted upon or otherwise considered.

(g) A working team document submitted to the Expert Panel is not a document of the Expert Panel unless and until the Expert Panel approves it. The Expert Panel may approve a working team document with or without revisions, may return the document to the working team for additional work consistent with the directions of the Expert Panel and the procedures described above, or may disapprove the document.

(h) Liaison members may describe to their constituencies the substance of a working team document, but may not quote from the document or make it available for reading or reproduction unless and until it is submitted to the Expert Panel and thereby becomes available for public disclosure. When a working team submits a document to the Expert Panel, the document becomes subject to the provisions of these procedures governing public availability of documents submitted to the Expert Panel and thereby becomes available for public disclosure (see Section 51).

## Section 44. Tentative Report of the Expert Panel.

(a) Prior to issuing a final report as described in Section 45 of these procedures, the Expert Panel shall issue a tentative report.

(b) The tentative report of the Expert Panel shall meet all of the requirements established for a final report in Sections 45(a) and (b) of these procedures.

(c) The public notice of the availability of the tentative report shall provide 90 days within which any interested person may submit comments on the tentative report and a request for oral hearing before the Expert Panel on the tentative report.

(d) An oral hearing shall be granted by the Expert Panel on a tentative report of the Expert Panel for good cause shown. Any such oral hearing shall be conducted pursuant to the provisions of Section 39 of these procedures.

## Section 45. Final Report of the Expert Panel.

(a) With respect to each cosmetic ingredient (or, where appropriate, closely related group of cosmetic ingredients), the Expert Panel shall issue a final report. The final report shall state the determination of the Expert Panel in accordance with Section 42 of these procedures with respect to each ingredient and any relevant conditions of its use.

(b) The final report shall contain the complete conclusions and recommendations of the Expert Panel with respect to the ingredient involved, including a full explanation of the reasons for those conclusions and recommendations and references to the scientific information on which the Expert Panel relies.

(c) The final report shall refer and respond to each point made in any submission or oral statement made with respect to the tentative report pursuant to Section 44 of these procedures.

(d) The Scientific Coordinator shall arrange for the publication of each final report in an appropriate scientific journal, and arrange for public dissemination of the final report.

## Section 46. Amendment of a Final Report.

(a) Any interested person who believes that a final report is incorrect may petition the Expert Panel to amend the final report to correct such error. The Director shall give public notice of any such petition and all proceedings of the Expert Panel with respect to any such petition shall be conducted pursuant to these procedures.

(b) A petition to amend a final report pursuant to this section shall ordinarily be based upon new data and information not previously reviewed by the Expert Panel. Such a petition shall be used primarily after the further data and information requested by the Expert Panel in the final report with respect to an ingredient, under each relevant condition of use, has been obtained, so that the Expert Panel can proceed with final determination with respect to that ingredient or condition.

(c) A determination by the Expert Panel with respect to a petition for amendment of the final report shall be handled in the same way as the initial determination by the Expert Panel. The Expert Panel shall first issue a tentative report in accordance with Section 44 and then a final report in accordance with Section 45.

## Part E — Public Notice and Availability of Records

### Section 50. Public Notice.

(a) The Director shall give public notice of the availability of all Scientific Literature Reviews, the meetings of the Expert Panel, decisions and reports of the Expert Panel, and all other similar information, in both of the following two ways:

(1) Such notice shall be mailed to a permanent mailing list consisting of representative members of the press (including interested newspapers, trade press, consumer publications, professional publications, and others) and representative interested organizations (including consumer, professional, and business organizations).

(2) Such notice shall also be given by mailing it to specific individuals who have demonstrated a continuing interest through direct participation in the Cosmetic Ingredient Review except for individuals who are members of organizations to which notice is provided.

(b) Any interested individual or organization may request that it be placed on the mailing list for all public notices by written application to the Director. Any such request shall be accompanied by a statement of the need of such individuals for such notices. The Steering Committee may, in its discretion, impose a fee for providing such notices to all individuals, which shall be no greater than the actual expenses involved in providing them.

## Section 51. Availability of Records for Public Disclosure.

(a) The following records relating to the Cosmetic Ingredient Review shall be available for public disclosure at the following time, except as otherwise provided in paragraph (b) of this section:

(1) The minutes of each Steering Committee meeting, after they have been approved by the Steering Committee and certified by the Steering Committee Chairman.

(2) Each Scientific Literature Review, at the time it is completed and available in printed form.

(3) Each chemical description, at the time it is submitted to the Director.

(4) Each submission of safety information pursuant to Section 30(e) of these procedures, at the time it is received by the Director.

(5) The written information made available for consideration by the Expert Panel at any meeting, at the same time that it is made available.

(6) Any transcript or recording of any open portion of an Expert Panel meeting, as soon as it is available.

(7) The minutes of any open portion of an Expert Panel meeting, after they have been approved by the Expert Panel and certified by the Expert Panel Chairman.

(8) All written data, information, or views submitted to the Expert Panel at any open portion of a meeting, as soon as they are so submitted.

(9) The minutes or portions thereof of any closed Executive portion of a meeting:

(i) For any matter not directed to be maintained as confidential pursuant to Section 31(h)(2) of these procedures, after they have been approved by the Expert Panel and certified by the Expert Panel Chairman.

(ii) For any matter directed to be maintained as confidential pursuant to Section 31(h)(2) of these procedures, after the matter relevant to those minutes, or portions thereof as acted upon by the Expert Panel or upon a determination by the Expert Panel that such minutes or portions thereof may be made available for public disclosure without undue interference with the operations of the Expert Panel.

(10) Any formal advice or report of the Expert Panel, after it has been issued by the Expert Panel.

(11) Any other Expert Panel records relating to the matter involved, except transcripts and recordings of closed portions of Expert Panel meetings, after the matter relevant to those records is acted upon by the Expert Panel, or upon a determination by the Expert Panel that such records may be made available for public disclosure without undue interference with the operations of the Expert Panel.

(b) The following records relating to the Cosmetic Ingredient Review shall not be available for public disclosure:

(1) Records relating to any cosmetic ingredient which has been determined by the Food and Drug Administration to be exempt from public disclosure pursuant to 21 C.F.R. 701.3(a) and 720.8(a).

(2) Adverse reaction reports, product experience reports, consumer complaints, and other similar data and information shall be available for public disclosure only in accordance with the regulations established by the Food and Drug Administration for public disclosure of such data and information in 21 C.F.R. 4.111(c)(3).

(3) All data and information relative to the nomination and selection of the members of the Expert Panel and liaison representative, in accordance with Section 21(e) of these procedures.

(4) A transcript or recording of any closed portion of an Expert Panel meeting, in accordance with Section 41(d) of these procedures.

(5) Documents of working teams of Expert Panel members which have not been submitted to the Expert Panel.

## Section 52. Public Documents Room.

(a) The Director shall establish a Public Documents Room, where one copy of all records available for public disclosure relating to the Cosmetic

Ingredient Review shall be stored and available for public review. The Public Documents Room shall have adequate space for interested persons to examine such documents.

(b) Any person who uses the Public Documents Room shall sign a log showing his name, affiliation, time of entry and exit, and a general description of the documents reviewed.

## Section 53. Public Inquiries and Requests for the Cosmetic Ingredient Review Records.

(a) Public inquiries on all matters relating to the Cosmetic Ingredient Review shall be directed to: Director, Cosmetic Ingredient Review, 1110 Vermont Ave., N.W., Suite 810, Washington, DC 20005, Telephone (202) 331-0651.

(b) All requests for records relating to the Cosmetic Ingredient Review, including records of the Expert Panel, shall be made to the Director.

(c) Copies of records that are publicly available pursuant to these procedures shall be made, upon request, for a fee that will reflect the actual cost of the labor and materials involved. The Director, with the approval of the Steering Committee, shall maintain a current price scheduled for such copying.

C I R

# Final Report
of the
Safety Assessment
for

prepared by
The Expert Panel
of the
Cosmetic Ingredient Review

A service to industry and consumers by
The Cosmetic, Toiletry and Fragrance Association

1110 Vermont Avenue, NW, Suite 810
WASHINGTON, DC 20005 202/331-0651

FINAL REPORT:KAREN BRANDT:pi:11/19/87

# METHYLENE CHLORIDE

November 19, 1987

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## ABSTRACT

$MeCl_2$ is a volatile compound that, if applied as an aerosol, would not remain on the skin for an extended period of time. However, certain cosmetic products that contain $MeCl_2$ are designed to remain on the skin and, thus may expose the skin to $MeCl_2$ for longer time periods. It has been estimated that the use of hair sprays containing $MeCl_2$ could expose the user to $MeCl_2$ concentrations ranging from 1 to 154 μg/liter of air.

$MeCl_2$ was irritating to the skin of animals; an antiperspirant and a deodorant containing $MeCl_2$ were mildly irritating to the skin of humans. Limited data obtained from animal and human studies indicated that $MeCl_2$ did not induce sensitization. No data were available on whether $MeCl_2$, when applied in a medium designed to remain on the skin is, or is not, a sensitizer. $MeCl_2$ does not absorb UVA or UVB light; therefore, it is unlikely to be a phototoxic agent.

In seven different laboratory studies with sufficient animals to permit meaningful statistical analysis of the data, only the results from a chronic mouse study - indicated that $MeCl_2$ is a carcinogen. Results of pharmacokinetic and metabolism studies established that the metabolism of $MeCl_2$ in the mouse differs quantitatively from other species studies, and this difference in metabolism could account for the positive tumorogenic response in the mouse. The available epidemilogical studies did not indicate a difference in cancer rates between exposed and unposed groups. To conclude that the one postive carcinogenicity study is of greater significance in safety evaluation than the six negative carcinogenicity studies, it would be necessary to exclude the results of the pharmacokinetic, metabolism and epidemological studies that support the conclusion that $MeCl_2$ is not a carcinogen for humans and other animal species. Considering all the data, and, in particular, the pharmacokinetic and metabolism data, it is concluded that data are insufficient to establish $MeCl_2$ as a human carcinogen. Further, it is also concluded that the positive carcinogenic response obtained in the mouse study cannot be extrapolated to humans. The evidence is that $MeCl_2$ is a carcinogen for mice, but is not carcinogenic for rats, hamsters or humans.

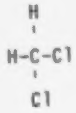
Due to the lack of human skin irritation and sensitization data on cosmetic products containing $MeCl_2$, the safety conclusion is restricted to aerosol products in which the duration of exposure (skin contact) is limited by the rapid evaporation of $MeCl_2$ from the skin.

On the basis of the data included in this report, it is concluded that $MeCl_2$ is safe for use in cosmetic products designed for brief discontinuous use.

## CHEMISTRY

### DESCRIPTION AND PROPERTIES

Methylene Chloride ($MeCl_2$) (Figure 1) is a disubstituted halogenated methane with the molecular formula, $CH_2Cl_2$, and CAS Registry No. 75-09-2. Synonyms for $MeCl_2$ include dichloromethane (IUPAC name) and methylene di(or bi)chloride (Hardie, 1964; Estrin et al., 1982a; Windholz et al., 1976).



$$\begin{array}{c} H \\ | \\ H-C-Cl \\ | \\ Cl \end{array}$$

Figure 1. Methylene Chloride

Physico-chemical properties of $MeCl_2$ are presented in Table 1. Reviews and monographs on $MeCl_2$ list additional properties (Hardie, 1964; International Agency for Research on Cancer [IARC], 1979; National Institute for Occupational Safety and Health [NIOSH], 1976; Environmental Protection Agency [EPA], 1985a). $MeCl_2$ is nonflammable and nonexplosive in air at room temperature (Windholz et al., 1976; Hawley, 1971). It is a colorless, volatile liquid that is soluble in alcohol, ether, acetone, carbon disulfide and dimethylformamide, and slightly soluble in water (2 g/100 ml at 20°C)(NIOSH, 1976; Weast, 1978).

$MeCl_2$ has no distinct absorption maxima in the visible wavelength range; its absorbance increases gradually at wavelengths shorter than 250 nm (Weast, 1978; National Toxicology Program [NTP], 1986).

The partition coefficient for $MeCl_2$ in an octanol/water system is 17.78 (Hansch et al., 1975). Those in blood/air, water/air, and blood/water systems are 7.9 ± 0.5, 7.2 ± 0.2, and 1.1, respectively (Lindqvist, 1978).

## TABLE 1

## PHYSICO-CHEMICAL PROPERTIES OF METHYLENE CHLORIDE

(Hardie, 1964; Windholz et al., 1976; Weast, 1978; World Health Organization [WHO], 1984)

| Property | | |
|---|---|---|
| Molecular Weight | | 84.94 |
| Boiling Point, °C, 760 mmHg | | 39.75 to 40.1 |
| Melting Point, °C | | -95 to -97 |
| Density | | $1.326_{4}^{20}$ |
| Vapor Density (a = 1) | | 2.93 |
| Vapor Pressure | | |
| | T°C | P mmHg |
| | 0 | 147.4 |
| | 10 | 229.7 |
| | 20 | 348.9 |
| | 25 | 436 |
| | 30 | 511 |
| | 35 | 600 |
| Log n-octanol:water partition coefficient | | 1.25 |
| Specific Gravity | | $1.33_{4}^{20}$ |
| Refractive Index, $n_{D}^{20}$, liquid | | 1.42 |
| Ignition Temperature, °C | | 624-662 |

## METHODS OF MANUFACTURE AND IMPURITIES

$MeCl_2$ can be formed by the chlorination of methane or methyl chloride, or by the reduction of chloroform or carbon tetrachloride (Hardie, 1964). Other laboratory methods for its preparation exist (Morrison and Boyd, 1973). The major manufacturing process utilizes the chlorination route followed by distillation for the isolation of $MeCl_2$ from the other alkyl chlorides formed (Hardie, 1964). In 1976, 65% of the $MeCl_2$ produced in the U.S. was obtained by the chlorination of methyl chloride. This process also yields chloroform and carbon tetrachloride (IARC, 1979; 1986).

Grades of $MeCl_2$ range from commercial and pesticide grades to highly purified spectrometric grades. The U.S. Pharmacopeia specifies the use of American Chemical Society (ACS) reagent grade $MeCl_2$ for pharmaceutical purposes (USP, 1980). Specifications for food and cosmetic grade $MeCl_2$ are presented in Table 2. Typical U.S. specifications for standard grade $MeCl_2$ are included in Table 2 for comparison.

Tentative Food and Agriculture Organization (FAO) specifications have been published (FAO, 1983) providing the accepted concentration in $MeCl_2$ of typical stabilizers. Maxima of 0.2% ethanol and of 50 mg/kg $C_5$ olefins are permitted. The Joint FAO World Health Organization (WHO) Expert Committee on Food Additives has requested more data on the nature, concentrations and methods of analysis for stabilizers and breakdown products in $MeCl_2$ (WHO, 1983; FAO, 1983).

Commercial grades of $MeCl_2$ may contain small quantities of stabilizers to prevent decomposition in air and moisture. Concentrations from C.0001 to 1.0% of phenolic compounds such as phenol, hydroquinone, resorcinol,

TABLE 2

SPECIFICATIONS FOR COSMETIC AND FOOD GRADE METHYLENE CHLORIDE

| Tests | Cosmetic Grade Specifications (Estrin et al., 1982b) | Food Grade Specifications* (FCC, 1981) | Standard Grade Specifications** (IARC, 1979) |
|---|---|---|---|
| Specific Gravity | 1.333 to 1.336 at 15°/4°C | 1.318 to 1.323 at 25°/25°C | 1.319 to 1.323 at 25°/25°C |
| Refractive Index at 20°C | 1.4232 to 1.4248 | approx. 1.424 | - - - |
| Boiling Range | 39.5° to 40.3°C | 39.5° to 40.5°C | 39.5° to 40.5°C |
| Acidity (as HCl) | 5.0 ppm max | 10 ppm max | 5 mg/kg max |
| Moisture | 80.0 ppm max | 0.02 percent max | - - - |
| Heavy Metals (as Pb) | - - - | 1 ppm max | - - - |
| Nonvolatile Residue | - - - | 0.002 percent max | 10 mg/kg max |

*Food Grade $MeCl_2$ must also pass a colorimetric test for the presence of free halogen.
**Standard Grade $MeCl_2$ must also be free of suspended matter and must have no free halogen (above detection limits).

thymol, 1-naphthol, amines, or a mixture of nitromethane and 1,4-dioxane have been used for this purpose (Hardie, 1964). Water acids and chloroform may also be present (Mercier et al., 1984).

Unidentified impurities were found in laboratory grade, distilled-in-glass grade, and HPLC grade $MeCl_2$ used in fluorometric and high performance liquid chromatographic (HPLC) analyses of biological samples (Kendall et al., 1968; Masoud et al., 1980). No impurities were detected in spectral quality grade $MeCl_2$. The concentrations of impurities in $MeCl_2$ varied between lots and manufacturing sources.

Impurities in different grades of $MeCl_2$ have been identified and quantified. Prolonged storage of $MeCl_2$ results in slow hydrolysis to formaldehyde (Lever, 1971). Cyanogen chloride was detected in several batches of a grade of $MeCl_2$ used as a solvent for drug and metabolite analysis (Franklin et al., 1978). One of 2 samples of "distilled-in-glass" grade $MeCl_2$ contained the impurities diethyl phthalate and dibutyl phthalate at concentrations of 0.52 and 7.7 mg/ml, respectively (Bowers et al., 1981). Pesticide grade $MeCl_2$ contained 22 impurities. The compounds, identified by mass spectrometry, were low molecular weight alkyl chlorides, phthalic anhydride and dioctyl phthalate. Container caps, inserts and liners were the suggested sources of phthalate for ether and anhydride formation.

Fourteen samples from 2 production lots of $MeCl_2$ from 1 manufacturer were analyzed for impurities over a 2-year period (Burek et al., 1984). A greater than 99% concentration of $MeCl_2$ was found in each sample.

Several lots of $MeCl_2$ were analyzed by gas chromatography-mass spectrometry for specific impurities (NTP, 1986). Although a few lots contained up to 14 impurities, only 5 impurities were identified and quantified. Less than 0.04% (v/v) vinylidene chloride, 0.0016% trans-1,2-dichloroethylene (in 1 sample), less than 0.005% carbon tetrachloride, less than 0.005% 1,2-dichloroethane, and less than 0.015% chloroform were detected. Other minor impurities accounted for less than 0.2% (combined relative area) of the major $MeCl_2$ peak in the gas chromatogram.

## ANALYTICAL CHEMISTRY

Gas chromatography is the most widely used method for $MeCl_2$ determination in environmental and biological samples (IARC, 1979; 1986). It is also used to analyze for purity of different grades and lots of $MeCl_2$ (Bowers et al., 1981; NTP, 1986). Techniques vary in the mode of sample preparation (Page and Charbonneau, 1984; Page and Kennedy, 1975), detection (DiPasquale et al., 1980; Schubert and Ketel, 1972) and in the type of adsorbent and carrier gas used (Vidal-Madjar et al., 1978; Schubert and Ketel, 1972; DiPasquale and Capaccioli, 1981). Modes of detection used currently are electron-capture or flame-ionization detection and mass spectrometry (NIOSH, 1976; EPA, 1984; Bowers et al., 1981).

Spectrophotometric methods for $MeCl_2$ identification include ultraviolet and infrared spectroscopy (NTP, 1986; Venable and Doyle, 1977). Nuclear magnetic resonance and mass spectra data have also been generated (NTP, 1986; Driscoll and Warneck, 1973). A chemical method for $MeCl_2$ quantitation involves the titration of free chloride ion released after the alkaline hydrolysis of $MeCl_2$ (Ratney et al., 1974).

## REACTIVITY AND STABILITY

The half-life of $MeCl_2$ in the troposphere is approximately 1 to 4 months (Dilling and Goersch, 1980). Major tropospheric photodecomposition products are carbon dioxide and hydrogen chloride; other products include carbon monoxide and phosgene ($COCl_2$). Reaction mechanisms and rates have been studied using simulated atmospheric conditions (Spence et al., 1976; Dilling et al., 1976; Vanlaethem-Meuree et al., 1978).

Alkyl halides such as $MeCl_2$ can undergo nucleophilic substitution and reduction (Morrison and Boyd, 1973). $MeCl_2$ hydrolyzes slowly at room temperature in the presence of moisture. Prolonged heating of $MeCl_2$ at temperatures from 140°C to 170°C yields formaldehyde and hydrochloric acid, and at 180°C yields formic acid, methyl chloride, methanol, hydrochloric acid and carbon monoxide. Significant chemical reactions of $MeCl_2$ have been reviewed (WHO, 1984; Hardie, 1964).

$MeCl_2$ reacts violently with lithium, sodium-potassium alloy, potassium tert-butoxide, a mixture of potassium hydroxide and N-methyl-N-nitrosourea (Sax, 1979) and with aluminum (Hardie, 1964). Eighteen hours of hydrolysis of $MeCl_2$ in potassium hydroxide released about 4% of the total amount of chlorine as titratable chloride ion; 20% was released after 96 hours of hydrolysis (Ratney et al., 1974).

$MeCl_2$ is reduced readily to methyl chloride and methane by alkali metal ammonium compounds in liquid ammonia. $MeCl_2$ is also halogenated to form compounds such as carbon tetrachloride and bromochloromethane or combined with aromatic compounds such as benzene and toluene to yield diphenylmethane and dimethylanthracene (Hardie, 1964).

Exposure of $MeCl_2$ to sources of intense heat such as flame, sparks, or red-hot surfaces will decompose the vapor and form toxic and corrosive gases (Conseil Europeen des Federations de l'Industrie Chimique [CEFIC], 1986).

## OCCURRENCE AND USE

### OCCURRENCE

$MeCl_2$ has been measured in the air and in water supplies at concentrations up to approximately 0.2 $mg/m^3$ and 2 µg/l, respectively. Its distribution varies with the latitude, elevation, and industrial environment (IARC, 1979; 1986; WHO, 1984).

Approximately 80% of the $MeCl_2$ produced is dispersed in the environment. However, the concentration of $MeCl_2$ in the troposphere is relatively low due to its reaction with hydroxyl radicals (Vanlaethem-Meuree et al., 1978). The lifetime of $MeCl_2$ in the troposphere was estimated at 3.6 months to 1 year.

Reported concentrations of $MeCl_2$ detected in ground and surface water ranged from trace quantities to 3.6 mg/l and to 13 µg/l, respectively (Brown et al., 1984). The occurrence of $MeCl_2$ in natural waters (Horvath, 1976) is not as well documented as is its occurrence in drinking water supplies or in effluents from manufacturing and processing plants. Chlorination of water containing organic compounds yielded $MeCl_2$ and other halogenated hydrocarbons (IARC, 1979; 1986; WHO, 1984).

Extent of exposure to $MeCl_2$ has been determined in several occupational environments (National Institute for Occupational Safety and Health [NIOSH], 1976). These environments have usually involved exposure not only to $MeCl_2$ but also to other hazardous solvents and gases (Strande, 1978).

Trace quantities of $MeCl_2$ were detected in the expired air of 5 unexposed male volunteers (Conkle et al., 1975) and in the arterial and placental blood samples of 11 unexposed pregnant female volunteers (Dowty et al., 1976).

## USE

$MeCl_2$ has industrial, medical, and home uses. It has been used as a solvent for the manufacture of other compounds, in degreasing and cleaning fluids, paint removers, refrigerants, and fumigants and in textile and leather coating (Windholz et al., 1976; Hawley, 1971; IARC, 1979; 1986; Grant, 1969; Fishbein, 1979; Hardie, 1964). The physico-chemical properties of $MeCl_2$ have resulted in the wide use of the solvent as a component of propellant systems in aerosol product formulations (Anthony, 1976a; IARC, 1979; 1986; Mercier et al., 1984).

Currently the regulated uses for $MeCl_2$ in foods include its use as a direct food additive (21 CFR 172.560, 173.255) in the extraction of modified hops extract from hops for beer, caffeine from coffee, and oleoresins from spice, use as an indirect food additive (21 CFR 175.105) in the formulation of adhesives, and use as a diluent in color additive mixtures for food use (21 CFR 73.1). Once a secondary solvent used to decaffeinate coffee (Valle-Riestra, 1974), $MeCl_2$ became the primary solvent substituting for trichloroethylene (Fishbein, 1979). Specifications for the use of $MeCl_2$ in foods have been published (Food Chemicals Codex [FCC], 1981).

$MeCl_2$ is listed as an "inactive ingredient" in approved prescription drug products exempt from FDA labeling requirements (Brown, 1983). $MeCl_2$

has been used as a clinical anesthetic as a result of its narcotic properties (Browning, 1965).

$MeCl_2$ has been used primarily by the cosmetic industry as a component of the aerosol propellant system in hair spray formulations. Other uses that have been reported to the Food and Drug Administration (FDA) by cosmetic manufacturers and formulators included use in manicuring and nail polish and enamel remover preparations and personal cleanliness products (FDA, 1981; 1985). $MeCl_2$ is also used in novelty temporary hair colorings applied as sprays (Fise, 1986).

Mixtures of propellants and other vapors and concentrates with $MeCl_2$ have been used in hair spray formulations. A typical formulation may contain propellants, such as isobutane, and $MeCl_2$ (Hoffman, 1973; Balsam and Sagarin, 1972), or may have consisted of a 50% hair spray concentrate in alcohol with compressed gases and haloalkanes such as $MeCl_2$ and trichloroethane (Wilkinson and Moore, 1982).

Concentrations of $MeCl_2$ in hair spray formulations have been reported to range from 10 to 20% (Balsam and Sagarin, 1972; Hoffman, 1973; Sayad et al., 1976; Anthony, 1976a; 1976b; Wilkinson and Moore, 1982). Data reported to FDA before and during 1981 and before and during 1985 (FDA, 1981; 1985) indicated that $MeCl_2$ concentrations in hairspray formulations ranged from 1 to 50%.

Product formulation data submitted to FDA in 1986 indicated that $MeCl_2$ was not used in any cosmetic products (FDA, 1986).

Voluntary filing of product formulation data with FDA by cosmetic manufacturers and formulators conforms to the tabular format listing preset ingredient concentration ranges and product categories in accordance with Title 21 section 720.4 of the Code of Federal Regulations (CFR, 1984). Since certain cosmetic ingredients are supplied by the manufacturer at less than 100% concentration, the value reported by the cosmetic formulator may not necessarily reflect the actual concentration found in the finished product; the actual concentration in such a case would be a fraction of that reported to the FDA. Data submitted within the framework of preset concentration ranges provide the opportunity for overestimation of the actual concentration of an ingredient in a particular product. An entry at the lowest end of a concentration range is considered the same as one entered at the highest end of that range, thus introducing the possibility of a 2- to 10-fold error in the assumed ingredient concentration.

The primary use of $MeCl_2$ was in hair spray formulations. $MeCl_2$ may contact the hair, skin, and possibly the respiratory tract and eyes under normal conditions of use. Hairsprays may be used once or twice daily and average spray time (i.e., time for application) ranges from 8 to 14 sec per application (CEFIC, 1986a; Battagello et al., 1984). Product formulations containing $MeCl_2$ may be used once a week to several times per day.

In a simulated study of $MeCl_2$ exposure of beauty salon operators, the time-weighted average (TWA) exposure to $MeCl_2$ for a typical operator was 6 ppm (Sayad et al., 1976). The hair spray tested contained $MeCl_2$, alcohol, and carbon dioxide at concentrations of 15.0, 80.0, and 5.0%, respectively. An average of 18 ppm $MeCl_2$ was detected in the breathing zone of the operator during spraying.

The air quality of a professional beauty salon was monitored while beauticians used hair spray products (Hoffman, 1973). One hair spray composition contained $MeCl_2$ at a concentration of 19%; other ingredients were propellants (73%) and isobutane (8%). The beauticians were exposed to daily mean concentrations of less than 1 to 2 ppm $MeCl_2$ over a 1-week period. Peak air samples of $MeCl_2$ taken a few minutes after hair spraying ranged from 1 to 130 ppm.

In an occupational use study, an aerosol containing 50% $MeCl_2$ was applied for 8 sec twice, with a 10 min interval between applications in a 25 $m^3$ room without ventilation (Battagello et al., 1984). A probe at the level of the respiratory ducts of the operator detected less than 60 ppm $MeCl_2$ at the peak of the first application and less than 80 ppm $MeCl_2$ at the peak of the second. $MeCl_2$ decreased to approximately 30 ppm by 10 min after the second exposure.

## REGULATORY REVIEW

Several government agencies are reviewing the risks to humans of exposure to $MeCl_2$. Current occupational and environmental standards for $MeCl_2$ use are based on the risk due to the toxicity of carbon monoxide derived from $MeCl_2$ metabolism rather than the putative mutagenic or carcinogenic activity of $MeCl_2$ itself (Laib, 1982).

The use of $MeCl_2$ in spray paints and paint strippers is being reviewed by the Consumer Products Safety Commission. Risks due to its occurrence in ambient air and water are being reviewed by the Environmental Protection Agency (EPA, 1984; 1985a; 1985b).

The Food and Drug Administration (FDA) has proposed to "ban the use of Methylene Chloride as an ingredient of cosmetic products..." but, based on the *de minimis* doctrine, to "permit the continued use of Methylene Chloride to decaffeinate coffee..." (Federal Register, 1985).

Evaluations of standards for occupational exposure to $MeCl_2$ are being performed by the National Institute for Occupational Safety and Health (NIOSH, 1976) and by the Occupational Safety and Health Administration. Current standards set a permissible exposure limit of 500 ppm $MeCl_2$ as an 8-hour TWA. An acceptable ceiling concentration of 1000 ppm and a maximal peak above this concentration of 2000 ppm for no more than 5 minutes in any 2 hours have been established (NIOSH, 1976; Mackison et al., 1978; Skrabalak and Babish, 1983). The American Conference of Governmental Industrial Hygienists (ACGIH) has recommended a TWA threshold limit value (TLV) of 100 ppm in the absence of exposure to carbon monoxide (ACGIH, 1980; 1985). NIOSH has recommended a TWA-TLV of 75 ppm, an exposure which "should not produce carboxyhemoglobin saturation levels greater than 5%" (NIOSH, 1976; DiVincenzo and Kaplan, 1981b). Standards in other countries range from 57 ppm in Rumania to 500 ppm in Japan and Germany (NIOSH, 1976).

## ABSORPTION, DISTRIBUTION, METABOLISM, AND EXCRETION

### ABSORPTION

The absorption of $MeCl_2$ has been studied after inhalation exposure in rats (McKenna et al., 1982; Stott and McKenna, 1984), mice (Bergman, 1983), dogs (MacEwen et al., 1972; DiVincenzo et al., 1972), and humans. Data primarily from human studies are presented in this section.

The amount of $MeCl_2$ absorbed has been measured in exhaled alveolar air or arterial blood samples using gas chromatography of $MeCl_2$ or scintillation counting of isotopically labeled $MeCl_2$. An inverse relationship was found between the percentage uptake of hydrophobic solvent (including $MeCl_2$) by humans and the quotient between concentration of the solvent in alveolar air and inspiratory air (Astrand and Gamberale, 1978).

The absorption of $MeCl_2$ by inhalation has logarithmic time course patterns. During exposure, the time course breath excretion curve has 2 phases: a rapid initial first-order uptake rate followed by a zero-order rate. The apparent steady-state $MeCl_2$ concentrations observed after 2 hours of inhalation exposure indicates a saturable absorption mechanism (DiVincenzo et al., 1972). While the shape of the absorption curve remains the same, there was a corresponding shift to higher concentrations with higher exposure concentrations. Increased duration of exposure had little or no effect on the absorption or accumulation of $MeCl_2$ (DiVincenzo and Kaplan, 1981a; Peterson, 1978; DiVincenzo et al., 1972).

The absorption of $MeCl_2$ by humans was influenced by pulmonary ventilation rate, membrane diffusion rate, and the relative solubility of $MeCl_2$ in blood and tissues (Astrand, 1975; DiVincenzo et al., 1972). Physical exercise during inhalation exposure of human subjects to $MeCl_2$ increased pulmonary absorption (Astrand et al., 1975; DiVincenzo and Kaplan, 1981b).

$MeCl_2$ absorption by humans correlated with lipid solubility (Morgan et al., 1972), degree of obesity, and body weight (Engstrom and Bjurstrom, 1977). Compared to other organic solvents, $MeCl_2$ was moderately water soluble and lipid soluble, properties which increased the probability of distribution to aqueous sites and accumulation in fatty tissue, respectively. Increased distribution and accumulation resulted in less available $MeCl_2$ vapor for pulmonary excretion.

Pulmonary absorption of $MeCl_2$ by sedentary humans has ranged from 55% to 70 to 72% of exposure concentrations up to 1740 $mg/m^3$ (Astrand et al., 1975; DiVincenzo and Kaplan, 1981a; 1981b). This range may be due to variations in exposure concentrations and schedules. Uptake of $MeCl_2$ by human subjects performing psychological tests increased from 130 mg after the first 30 min exposure period at 870 $mg/m^3$ $MeCl_2$ to 1145 mg after the fourth period at 3470 $mg/m^3$ $MeCl_2$ (Astrand and Gamberale, 1978). Impairment of performance was observed when uptake of $MeCl_2$ was 1145 mg; impairment of performance occurred at lower concentrations of toluene, methylchloroform, trichloroethylene and styrene. Absorption rates ranged from 0.31 to 1.43 mg/min during exposure to 74 to 333 $mg/m^3$ $MeCl_2$ (Perbellini et al., 1977).

Results of in vitro studies indicated greater skin penetration by $MeCl_2$ than by other halogenated hydrocarbons (Stewart and Dodd, 1964). Percutaneous absorption rates of 1291 $nmol/min/cm^2$ through mouse abdominal skin and 1140 $nmol/min/cm^2$ through rat skin were measured for $MeCl_2$ (Tsuruta, 1975; 1977). Other halogenated hydrocarbons tested included tetrachloroethylene, chloroform and carbon tetrachloride. Compounds with the highest solubilities in water (highest water:air partition coefficients) had the greatest absorption rates (Tsuruta, 1975).

Within 24 hours of the intraperitoneal administration to rats of 412 to 930 mg/kg $^{14}C$-$MeCl_2$, radioactivity was detected in the breath, urine, feces, and carcasses (DiVincenzo and Hamilton, 1973). Gastric absorption of $MeCl_2$ from different vehicles was studied using rats (Withey et al., 1983). The uptake rate of $MeCl_2$ from an aqueous preparation was more rapid and gave rise to higher peak blood concentrations of $MeCl_2$ than that from a corn oil preparation. A series of uptake pulses rather than linear uptake was observed following absorption of $MeCl_2$ from the corn oil preparation. Similar uptake of $MeCl_2$ from the two vehicles was observed indicating greater solubility of $MeCl_2$ in water than the other solvents tested.

The absorption of $MeCl_2$, factors affecting uptake and retention, effects of variations in exposure regimes, and interspecies comparisons have been reviewed (Astrand, 1975; Thomas, 1975; Carlsson, 1982; Sato and Nakajima, 1979; Brown et al., 1984).

## DISTRIBUTION

### RATS

Inhalation exposure of rats to 50, 500, or 1500 ppm $^{14}C\text{-}MeCl_2$ for 6 hours resulted in overall tissue retention ranging from 23% of the total body burden after the 50 ppm exposure to 7% after the 1500 ppm exposure (McKenna et al., 1982). Blood concentrations of radioactive $MeCl_2$ reached apparent steady-state after 2 hours of exposure and declined exponentially after termination of exposure. The highest concentrations of radioactivity were found in the liver, kidneys and lungs of rats exposed to 50 to 1500 ppm $^{14}C\text{-}MeCl_2$ (McKenna et al., 1982). A 1-hour exposure to 1935 $mg/m^3$ $MeCl_2$ resulted in high concentrations of radioactivity in white adipose tissue and the adrenal glands, as well as in the liver and kidneys (Carlsson and Hultengren, 1975). Elimination of 25 to 90% of the accumulated radioactivity from these tissues was observed within 2 hours after the exposure.

Rats were exposed to 500 and 1000 ppm $MeCl_2$ and to 1000 ppm TWA $MeCl_2$ 6 hours per day for 1 or 2 weeks (Savolainen et al., 1981). The effects of dose and duration as well as exposure conditions on the accumulation of $MeCl_2$ in the brain and peri-renal fat of the rats were studied. The 1000 ppm TWA of $MeCl_2$ was achieved by exposing rats to 2 1-hour peak concentrations of 2800 ppm while maintaining a basal exposure level of 100 ppm $MeCl_2$ throughout the exposure period. Significant increases in $MeCl_2$ concentrations were measured in peri-renal fat after a 1-week exposure and in the brain after 1- and 2-week exposures to 1000 ppm TWA $MeCl_2$ in comparison with concentrations observed after exposures to 1000 ppm $MeCl_2$.

Logarithmic accumulation of $MeCl_2$ in peri-renal fat of rats was observed after intermittent inhalation exposure of 200 and 500 ppm $MeCl_2$ for 6 hr per day for 5 days. A logarithmic relationship between $MeCl_2$ accumulation in the brain and its concentration in adipose tissue was also observed (Savolainen, 1981).

Inhalation exposure of female rats to $MeCl_2$ during gestation resulted in fetal exposure to both $MeCl_2$ and carbon monoxide (CO) (Anders and Sunram, 1982). Transplacental distribution of $MeCl_2$ and CO was studied using rats exposed to 507 ppm $MeCl_2$ or 22 ppm CO for 1 hour on the 21st day of gestation. Exposure to both $MeCl_2$ and CO resulted in similar CO concentrations in maternal blood. $MeCl_2$ crossed placental membranes; however, the similar concentrations of CO in maternal and fetal blood indicated that the maternal liver was the major site of $MeCl_2$ metabolism.

Although the CO that formed equilibrated between maternal and fetal circulation, the greater concentration of CO in fetal blood after CO administration indicated greater affinity for CO by fetal hemoglobin.

Overall tissue retention of radioactivity was less than 10% in rats given doses of either 1 or 50 mg/kg $^{14}C-MeCl_2$ in distilled water by gavage (McKenna and Zempel, 1981). At both doses, the liver, kidneys and lungs had the highest concentrations of radioactivity, and epididymal fat had the lowest. Radioactivity was also measured in the brain, skeletal muscle, testes, whole blood, and the carcass.

Intraperitoneal administration of 412 to 930 mg/kg $^{14}C-MeCl_2$ to rats resulted in widespread dissemination of radioactivity in tissues although overall uptake of radioactivity was low (DiVincenzo and Hamilton, 1975). Highest tissue-specific activities were measured in the liver, kidneys, and adrenal glands. No significant accumulation was observed in the fat.

An uptake rate coefficient for peri-renal fat was determined from data on intravenous administration of 3 to 15 mg/kg doses of $MeCl_2$ to rats (Withey and Collins, 1980).

Relative liquid:air and tissue:air (tissue homogenized in 1:3 w:v ratio using 0.9% saline) partition coefficients were determined for $MeCl_2$ and other halogenated hydrocarbons in rats after inhalation exposure (Gargas et al., 1986). Relative solubilities in blood, 0.9% saline, olive oil, fat, liver, and muscle were:

$$CH_2Br_2>CH_2BrCl>CH_2Cl_2>CH_2FCl>CH_2F_2.$$

$MeCl_2$ was more soluble in olive oil and fat than in blood, liver, muscle, or saline.

MICE

Relative tissue distributions of radioactive $MeCl_2$ and other chlorinated hydrocarbons in mice after inhalation exposure were determined by whole-body autoradiography (Bergman, 1978; 1979; 1983; Bergman et al., 1981). Radioactivity from $^{14}C$-$MeCl_2$ was detected in the bronchi, liver and kidneys of treated mice. Other chlorinated hydrocarbons, such as chloroform and trichloroethylene, had different distribution patterns (Bergman, 1978). In general, the chlorinated hydrocarbons had longer body retention times in mice than did other organic solvents such as benzene, toluene, and styrene (Bergman, 1979).

Results of other autoradiographic studies confirmed the localization of radioactivity from $^{14}C$-$MeCl_2$ in the liver, kidneys, and bronchi of treated mice (Bergman, 1983). Radioactivity was also concentrated in the lungs, body fat, blood, white matter of the brain, spinal cord, and nerves of the mice. The high content of radioactivity in blood up to 4 hours following exposure was considered to be $^{14}C$-carboxyhemoglobin. Nonvolatile radioactivity was localized in tissues with rapid cell turnover or high rates of protein synthesis such as the liver, bronchi, and kidneys, and volatile radioactivity was localized in fatty and nervous tissue.

Hepatic radioactivity was nonextractable (covalently bound) and was not localized in the centrilobular hepatocytes where the microsomal P-450 system is found. The uniform hepatic distribution of radioactivity indicated possible non-specific cytosolic distribution. In vitro covalent binding of $^{14}C$-$MeCl_2$ metabolites to hepatic microsomal proteins and lipids has been demonstrated (Anders et al., 1977; Sipes and Gandolfi, 1980). In contrast to other halogenated hydrocarbons, $MeCl_2$ metabolites had the least binding to microsomal protein, little binding to lipids, and negligible binding to DNA (Sipes and Gandolfi, 1980). The *in vitro* alkylation of hepatic subcellular macromolecules could not be confirmed *in vivo* using rats given $^{14}C-MeCl_2$ by gavage (McKenna and Zempel, 1981).

Data from tissue distribution studies with mice and rats indicated greater accumulation of radioactivity in the liver and kidneys and more rapid elimination of radioactivity from body fat and the brain in comparison with other tissues (Bergman, 1983).

## HUMANS

During acute and repeated inhalation exposures of human subjects to 50 to 200 ppm $MeCl_2$, the concentrations of $MeCl_2$ in the blood increased gradually over time and eventually reached a plateau. The concentration in the blood during exposure was related to the exposure concentration (DiVincenzo and Kaplan, 1981a).

Approximately 100 to 450 mg of the total uptake of 1300 mg of $MeCl_2$ was measured in the adipose tissue of human subjects exposed to 2600 mg/$m^3$ in inspired air (Engstrom and Bjurstrom, 1977). Although slim subjects had 2-fold higher $MeCl_2$ concentrations per gram adipose tissue than obese subjects, the latter had higher total body $MeCl_2$ concentrations. Mean $MeCl_2$ concentrations in adipose tissue of the 12 subjects was approximately 9.4 mg/kg (estimated from figures) at time zero (when exposure was concluded) and was 10.2 mg/kg and 8.4 mg/kg 1 hour and 4 hours, respectively, after the exposure was terminated.

Physical exercise and smoking during and after an acute inhalation exposure to 100 ppm $MeCl_2$ markedly increased $MeCl_2$ concentrations in the blood of human subjects. Elimination time course curves of $MeCl_2$ from the blood of exercising subjects were similar to those of sedentary subjects. Rapid disappearance of $MeCl_2$ from the blood of smoking and nonsmoking subjects was observed at the termination of exposure; blood concentrations of $MeCl_2$ decreased below detection limits within the following 16 hours (DiVincenzo and Kaplan, 1981b).

Eleven pairs of maternal and placental cord blood samples were collected at birth from normal human patients and were analyzed by gas chromatography (Dowty et al., 1976). Although these patients had undergone no experimental treatment, the presence of $MeCl_2$ and more than 100 other volatile organic compounds was detected.

## METABOLISM

### METABOLISM TO CARBON MONOXIDE AND CARBON DIOXIDE

Significantly elevated concentrations of carbon monoxide (CO) were detected in the breath, and carboxyhemoglobin (COHb) in the blood of humans after exposure to $MeCl_2$ by inhalation (Stewart et al., 1972a; 1972b; Stewart and Hake, 1976). Home use of $MeCl_2$ as a solvent in paint remover has also been associated with elevated carboxyhemoglobin values (Stewart and Hake, 1976). Most data from studies of inhalation exposure of rabbits (Roth et al., 1973; 1975; Boudene, 1978), rats (Carlsson and Hultengren, 1975; Ciuchta et al., 1979; Kim and Carlson, 1986), monkeys (Ciuchta et al., 1979), and humans (Ratney et al., 1974; Putz et al., 1979; DiVincenzo and Kaplan, 1981a; Stewart et al., 1983) indicated that $MeCl_2$ exposure resulted in elevated CO concentrations as a result of metabolic conversion of $MeCl_2$ to CO.

However, an inhalation study in which humans were exposed to an average of 450 ppm $MeCl_2$ in an aerosol paint product for 26 minutes resulted in no measurable increase in the COHb concentration in the blood of 12 subjects (Stevenson et al., 1978). In another study of simulated occupational inhalation exposure of hair salon operators to $MeCl_2$ in a hair spray formulation, environmental conditions other than $MeCl_2$ inhalation, such as smoking, produced higher COHb concentrations than exposure to approximately 400 ppm $MeCl_2$ (Sayad et al., 1976).

An alternate hypothesis has been proposed. Based on data from X-ray crystallographic and diffraction, and nuclear magnetic resonance spectrometric studies, an increase in the affinity of hemoglobin and myoglobin for endogenous CO (not derived from $MeCl_2$)(Nunes and Schoenborn, 1973; Settle, 1975) or a decrease in affinity for oxygen (Harkey et al., 1979; Saxena et al., 1982; Ott et al., 1983) was suggested to result from the allosteric binding of $MeCl_2$ at specific site(s) on hemoglobin (Schoenborn, 1976; Saxena et al., 1982). However, it has been widely accepted that $MeCl_2$ acts as a direct substrate for metabolic formation of CO (Rodkey and Collison, 1977a; Collison et al., 1977; Dill et al., 1978; Laib, 1982).

Although CO has been measured in the breath and COHb in the blood, no increase in dissolved CO in the blood of humans has been reported after $MeCl_2$ exposure (Lanhennig et al., 1976).

The COHb produced from inhaled $MeCl_2$ at doses up to 500 ppm had a biologic half-life twice that of COHb from exogenous CO in humans (Stewart et al., 1983). The prolonged half-life of CO and COHb produced after $MeCl_2$ exposure in comparison with that of endogenous CO (Stewart et al., 1972a; 1973; Carlsson and Hultengren, 1975) was considered due to continued CO formation in the liver from the $MeCl_2$ accumulated in and redistributed from other tissues (Benzon et al., 1978; McKenna et al., 1982). The formation of CO and high concentrations of COHb were decreased to pre-exposure concentrations once the supply of $MeCl_2$ to the liver declined or when the respiratory clearance of $MeCl_2$ exceeded the redistribution process. The contribution of residual post-exposure metabolism to total metabolite production was greater for lipophilic compounds with low volatility (Andersen, 1981a).

Using metabolic conversion data from inhalation exposure studies with rats, empirical molar ratios of $MeCl_2$ to CO and to carbon dioxide ($CO_2$) were 1:0.48 and 1:0.3, respectively (Rodkey and Collison, 1977a; 1977b). In studies with hepatic microsomal fractions from rats, $^{14}CO$ was identified as the principal and $^{14}CO_2$ as a minor microsomal metabolite of $^{14}C\text{-}MeCl_2$ (Kubic and Anders, 1978). Calculated mean _in vitro_ microsomal $^{14}CO$ and $^{14}CO_2$ production rates of 3 samples each were 16.7 and 0.2 nmol/mg protein/min, respectively (Anders et al., 1978; Kubic and Anders, 1978). The final concentration of $^{14}C\text{-}MeCl_2$ in hepatic microsomal preparations was 48 mM (sp. act. 26 μCi/mmol). _In vivo_ metabolic rates for rats inhaling 50 and 1500 ppm $MeCl_2$ for 6 hours were 0.57 and 2.8 nmol/min/g body weight, respectively (Landry et al., 1983).

Metabolic conversion of $MeCl_2$ to CO, COHb, and $CO_2$ has been studied in several species (Table 3). In a recent study, COHb saturation concentrations following a single 12-h exposure were not different significantly from those following an 8-h exposure of Swiss Webster mice and Sprague-Dawley rats to 200, 500 and 1000 ppm $MeCl_2$ (Kim and Carlson, 1986). Repeated exposure for

TABLE 3

CO AND COHb PRODUCTION AFTER METHYLENE CHLORIDE ADMINISTRATION

| Concentration of $MeCl_2$ | Species | Exposure Regimen | Results | Reference |
|---|---|---|---|---|
| | | | INHALATION STUDIES | |
| 50 ppm<br>500 ppm<br>1500 ppm | rat<br>rat<br>rat | 6-hr exposure<br>6-hr exposure<br>6-hr exposure | 3 percent COHb sat'n level<br>10-13 percent COHb level<br>10-13 percent COHb level | McKenna et al., 1982 |
| 440 to 2300 ppm | rat | 3-hr exposure | at 440 ppm: Δ percent - 7 percent during and after exposure<br>same Δ percent COHb at higher concentration except prolonged effect | Hogan et al., 1976 |
| 80 to 800 μmol/kg | rat | single dose, 7-hr exposure | 35-fold increase in CO-production rate over endogenous rate (16 ± 0.5 μmol/kg/day or 0.67 μmol/kg-hr)<br>Empirical Molar Ratio of $MeCl_2$:CO - 1:0.48 | Rodkey and Collison, 1977b |
| 0.2 mmol/kg | rat | single dose, 7-hr exposure | 76 percent of radioactivity → $^{14}CO$ and $^{14}CO_2$<br>47 percent of 76 percent - $^{14}CO$<br>~ 29 percent of 76 percent - $^{14}CO_2$<br>Empirical Molar Ratios:<br>$MeCl_2$:CO - 1:0.5<br>$MeCl_2$:$CO_2$ - 1:0.3 | Rodkey and Collison, 1977a |
| 200 ppm | rat | 8 hr/d, 5 d or 12 hr/d, 4 d | No COHb detected before study<br>~ 10 percent COHb after 1st d<br>~ 8 percent COHb after 4d/5d<br>~ 2 percent COHb after study | Kim and Carlson, 1986 |
| 500 ppm | rat | 8 hr/d, 5 d or 12 hr/d, 4 d | No COHb detected before or after study<br>~ 8-10 percent COHb after 1st d<br>~ 9-11 percent COHb after 4d/5d | Kim and Carlson, 1986 |
| 1000 ppm | rat | 8 hr/d, 5 d or 12 hr/d, 4 d | No COHb detected before study<br>~ 13-14 percent COHb after 1st d<br>~ 9-11 percent COHb after 4d/5d<br>~ 2 percent COHb after study | Kim and Carlson, 1986 |

TABLE 3 - Continued

CO AND COHb PRODUCTION AFTER METHYLENE CHLORIDE ADMINISTRATION

| Concentration of $MeCl_2$ | Species | Exposure Regimen | Results | Reference |
|---|---|---|---|---|
| 200 ppm | mouse | 8 hr/d, 5 d or<br>12 hr/d, 4 d | - 1 percent COHb before study<br>- 9 percent COHb after 1st d<br>- 10 percent COHb after 4d/5d<br>- 2 percent COHb after study | Kim and Carlson, 1986 |
| 500 ppm | mouse | 8 hr/d, 5 d or<br>12 hr/d, 4 d | - 1 percent COHb before study<br>- 16 percent COHb after 1st d<br>- 12-17 percent COHb after 4d/5d<br>No COHb after study | Kim and Carlson, 1986 |
| 1000 ppm | mouse | 8 hr/d, 5 d or<br>12 hr/d, 4 d | - 1 percent before study<br>- 15-16 percent COHb after 1st d and 4d/5d<br>- 2 percent COHb after study | Kim and Carlson, 1986 |
| 500-7000 ppm | rabbit | 1-hr exposure | Relationship between CO and $MeCl_2$ exposure: Effect of 100 ppm $MeCl_2$ = Effect of 50 ppm CO | Boudene, 1978 |
| 100 ppm<br>200 ppm | human | 8-hr time-weighted average (TWA) | 2.8 percent COHb sat'n level<br>5.1 percent COHb sat'n level | Ott et al., 1983a |
| 180 to 200 ppm | human | occupational exposure | - 4.5 percent COHb sat'n level at beginning of workday<br>- 9 percent COHb sat'n level after 8-hr exposure wh/exponentially decayed to 4.5 percent by next day<br>7.3 percent COHb sat'n = 24-hr Time-Weighted-Average percent COHb | Ratney et al., 1974 |

TABLE 3 - Continued

CO AND COHb PRODUCTION AFTER METHYLENE CHLORIDE ADMINISTRATION

| Concentration of $MeCl_2$ | Species | Exposure Regimen | Results | Reference |
|---|---|---|---|---|
| 200 ppm | human | 4-hr exposure | Inhaled either 200 ppm $MeCl_2$ or 50 ppm CO, increased COHb from 1.35 to 5.0 percent<br>Note: 70 ppm CO exposure produced 45-47 ppm CO in body and increased COHb from 1.5 to 4.85 percent<br>Controls: 12 ppm CO and 1.4 - 1.6 percent COHb | Putz et al., 1979 |
| 50 ppm<br>100 ppm<br>150 ppm<br>200 ppm | human | 7.5-hr exposure or 7.5-hr/d, 5 d exposure | Peak Blood COHb: 1.9 percent<br>3.4 percent<br>5.3 percent<br>6.8 percent<br>Marginal increase in COHb with repeated exposure up to 5 days<br>Of 70 percent absorbed (vs. inspired), 25-34 percent expired as CO during and after exposure<br>To achieve a 5 percent COHb sat'n level: an 8-hr exposure to ~150 ppm $MeCl_2$ = an 8-hr exposure to 35 ppm CO | DiVincenzo and Kaplan, 1981a |
| 0 to 500 ppm | human | 7.5 hr/d, 5 d/wk, 6 wk exposure to steadily increasing concentrations | In nonsmokers: increased percent COHb from 0.8 percent to 11.4 percent on 6th wk<br>In light smokers: increased percent COHb from 1.5 percent to 12.1 percent on 6th wk | Stewart et al., 1973 |
| 0 to 500 ppm | human | 3 hr/d, 5 d/wk, 6 wk exposure to steadily increasing concs | In nonsmokers: increased percent COHb from 1.0 percent to 7.3 percent on 6th wk<br>In "garageman": increased from 1.2 percent to 6.0 percent on 6th wk<br>In heavy smoker: increased from 6.2 percent to 11.9 percent on 6th wk | Stewart et al., 1973 |
| 29 percent $MeCl_2$ in aerosol formulation (~450 ppm $MeCl_2$ over a 26-min exposure) | human | Home-use exposure | In nonsmokers: increased percent COHb from 1.0 percent to 1.8 percent<br>(Control nonsmokers: no change)<br>In smokers: increased percent COHb from 0.8 percent to 4.2 percent<br>(Control smokers: 1.2 to 1.7 percent COHb) | Stevenson et al., 1978 |

TABLE 3 - Continued

CO AND COHb PRODUCTION AFTER METHYLENE CHLORIDE ADMINISTRATION

| Concentration of $MeCl_2$ | Species | Study Type | Exposure Regimen | Results | Reference |
|---|---|---|---|---|---|
| | | | | OTHER STUDIES | |
| 3.0 mmol/kg | rat | intraperitoneal | single injection | 8 percent COHb sat'n level after 2 hrs (vs diff. maximal COHb levels at diff times for $MeBr_2$, $MeI_2$ . | Kubic et al., 1974 |
| 1 mg/kg | rat | oral | single dose | ~88 percent of dose metabolized<br>Relative percentage recovery of $^{14}CO_2$:$^{14}CO$ = 1.13 | McKenna and Zempel, 1981 |
| 50 mg/kg | rat | oral | single dose | ~28 percent of dose metabolized<br>Relative percentage recovery of $^{14}CO_2$:$^{14}CO$ = 0.5 | McKenna and Zempel, 1981 |

4 to 5 days did not result in increased COHb levels, and the dose-response relationship between $MeCl_2$ exposure and COHb formation was not linear.

The dose-response characteristics of $MeCl_2$ exposure in several species were influenced by the metabolism of $MeCl_2$ by saturable, enzyme-mediated pathways (McKenna et al., 1982; DiVincenzo and Kaplan, 1981a). Generally, exposure to increasing $MeCl_2$ concentrations resulted in increased CO and COHb concentrations. As exposure concentration increased, however, the CO and COHb concentrations increased to a lesser extent. Beyond a "threshold" concentration, more $MeCl_2$ and less CO and $CO_2$ were exhaled, a response that is indicative of saturation of the metabolic pathways of $MeCl_2$. Exposure to a constant $MeCl_2$ concentration resulted in increasing CO concentration over time. No saturation of $MeCl_2$ metabolic pathways and no plateau in CO concentration time course was observed at $MeCl_2$ concentrations below approximately 200 ppm in humans (DiVincenzo and Kaplan, 1981a); however, the apparent zero-order kinetics of $MeCl_2$ conversion was approached at higher $MeCl_2$ concentrations. The corresponding "threshold" $MeCl_2$ concentration in rats was between 50 and 500 ppm, but a specific concentration was not reported since only extremes of concentration were tested (McKenna et al., 1982).

The rate and extent of CO accumulation appeared to be similar in rats administered $MeCl_2$ intraperitoneally and by inhalation (Rodkey and Collison, 1977b). Increased concentrations of CO in exhaled air and COHb in blood were observed after intraperitoneal administration of $MeCl_2$ (Kubic et al., 1974; DiVincenzo and Hamilton, 1975). However, unlike inhalation exposure, repeated intraperitoneal administration of $MeCl_2$ was observed to substantially increase COHb concentrations (Kubic et al., 1974). In addition, $MeCl_2$ metabolism to formaldehyde has not been demonstrated following intraperitoneal administration of $MeCl_2$ (DiVincenzo and Hamilton, 1975).

The metabolic fate of orally administered $MeCl_2$ in mice and rats was related to dose; small doses were metabolized more extensively than were large doses (Yesair et al., 1977; McKenna and Zempel, 1981). Relative recoveries of CO and $CO_2$ were also dose-dependent (McKenna and Zempel, 1981).

## FACTORS INFLUENCING CO LEVELS DURING $MeCl_2$ METABOLISM

Other factors that influence the metabolism of $MeCl_2$ have been studied. A steadily increasing CO-production rate in rats exposed to 793 µmol/kg of $MeCl_2$ indicated possible substrate-induced enzyme formation (Rodkey and Collison, 1977b). Repeated inhalation exposures over several days resulted in a marginal increase in COHb saturation concentrations (DiVincenzo and Kaplan, 1981a); exposures over several weeks resulted in increased COHb saturation concentrations which returned to pre-exposure concentrations within a few days (Stewart et al., 1973).

An additive effect was found between CO resulting from exposure to $MeCl_2$ and endogenous concentrations of CO (Miller, 1984). Exogenous sources of CO other than $MeCl_2$ exposure include cigarette smoke and automobile exhaust.

Because of the affinity of CO for hemoglobin, the ability of CO to displace bound oxygen, and the stability of the COHb complex, humans exposed to CO and CO-producing compounds are at risk. Since COHb concentrations greater than 5% are thought to increase greatly the risk of angina pectoris and coronary infarctions by decreasing the available oxygen supply in the blood and also in the myoglobin of heart muscle (Miller, 1984), individuals with cardiovascular problems are vulnerable to $MeCl_2$ toxicity due to CO production (Ott et al., 1983a; Skrabalak and Babish, 1983). Furthermore, long-term neurological damage due to transient brain ischemia resulting from CO exposure has been indicated (International Congress of the European Association of Poisons Control Centres, 1985).

Endogenous COHb saturation levels of non-smoking humans range from 0.1 to 2.9%; those of smokers range from 2 to 8%, reaching concentrations of greater than 10% in heavy smokers (Stewart et al., 1973; Stevenson et al., 1978; Putz et al., 1979; DiVincenzo and Kaplan, 1981a; 1981b; Ott et al., 1983a). Smokers had higher overall COHb saturation levels following inhalation exposure to $MeCl_2$ in several studies (Stevenson et al., 1978; DiVincenzo and Kaplan, 1981b). Moreover, CO was detected immediately in their breath compared to the 30-min delay before detection in exposed non-smokers (Nakaaki et al., 1982). In addition, active smoking during exposure to $MeCl_2$ by inhalation greatly increased the COHb effect (Stevenson et al., 1978; DiVincenzo and Kaplan, 1981b). The COHb concentration in the blood of a heavy smoker actually decreased during exposure because the subject was prevented from smoking during the experiment (Stewart et al., 1973).

An increase in $MeCl_2$ metabolism to CO was observed in humans performing physical work during inhalation exposure in comparison with sedentary exposed subjects (DiVincenzo and Kaplan, 1981b). No increase in formaldehyde or formic acid concentration was observed in the blood or urine of the exposed, exercising subjects.

Simultaneous exposure to other compounds, such as toluene, ethanol, methanol or isopropanol, during $MeCl_2$ exposure decreased the levels of COHb in rats and monkeys (Ciuchta et al., 1979). The potentiation of the COHb effect by methanol during $MeCl_2$ exposure was not observed in humans. In addition, greater cardiac sensitivity to epinephrine was observed in humans during an 8-hour TWA of 140 to 475 ppm $MeCl_2$ (Ott et al., 1983a).

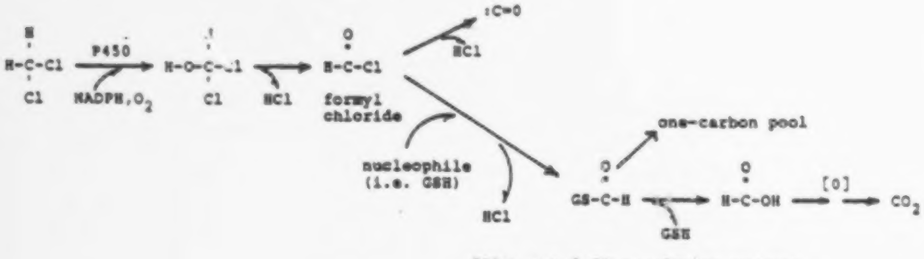
## MECHANISMS OF $MeCl_2$ METABOLISM

Two major pathways for $MeCl_2$ metabolism have been proposed. The first pathway, localized in the hepatic microsomal fraction, was mediated by a cytochrome P-450-dependent monooxygenase system (P450) and produced CO. The second pathway, found in the hepatic cytosolic fraction, was mediated by glutathione transferase (GT) and produced formaldehyde, formic acid and inorganic chloride, as well as $CO_2$ (Hogan et al., 1976; Anders et al., 1977). The 2 pathways are designated Pathways 1 and 2, respectively, and are presented in Figure 2.

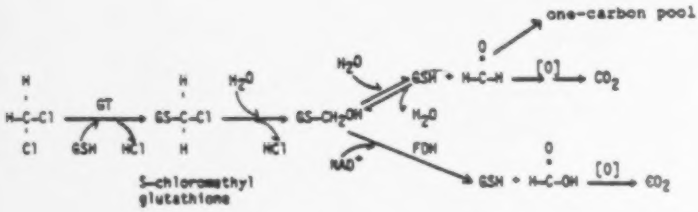
In vitro studies with hepatic microsomes from rats have been used to trace the metabolic conversion of $MeCl_2$ to CO by Pathway 1 (Fig. 2). This conversion required the cofactor, NADPH, and molecular oxygen (Kubic and Anders, 1975). In a closed atmosphere inhalation study with Fischer-344 rats (strain CDF F-344 CrlBR), the maximum metabolic rate for 100 to 300 ppm $MeCl_2$ by Pathway 1 was estimated to be 47 µmol/kg/h (Gargas et al., 1986). The accepted mechanism for the series of reactions in Pathway 1 involved an initial NADPH-dependent addition of $O_2$-derived monoatomic oxygen to $MeCl_2$,

Figure 2. Proposed Mechanisms for Methylene Chloride Metabolism.
(adapted from Anders et al., 1977; Gargas et al., 1986)

Pathway 1: P450-mediated, CO-producing pathway.


:C=O
HCl
H-C-Cl
Cl
P450
NADPH,$O_2$
H-O-C-Cl
Cl
HCl
H-C-Cl
formyl chloride
nucleophile (i.e. GSH)
HCl
one-carbon pool
GS-C-H
GSH
H-C-OH
[O]
$CO_2$

"Alternate" $CO_2$-producing pathway
(Gargas et al., 1986)


one-carbon pool
H-C-Cl
Cl
GT
GSH
HCl
GS-C-Cl
H
$H_2O$
HCl
GS-$CH_2$OH
$H_2O$
GSH + H-C-H
[O]
$CO_2$
$H_2O$
FDH
$NAD^+$
GSH + H-C-OH
[O]
$CO_2$
S-chloromethyl glutathione

Pathway 2: GSH-dependent, formaldehyde-, formic acid- and $CO_2$-producing pathway.

Key to Figure 2:

| | |
|---|---|
| FDH | formaldehyde dehydrogenase |
| GSH | reduced glutathione |
| GT | glutathione transferase |
| MFO | mixed function oxidase system |
| $NAD^+$ | oxidized nicotinamide adenine dinucleotide |
| NADPH | reduced nicotinamide adenine dinucleotide phosphate |
| [O] | oxidation reaction(s) |

followed by rearrangement to form a formyl chloride intermediate that decomposed to form CO (Anders et al., 1977). However, it has been proposed recently that a significant percentage (~ 20 to 30%) of the formyl chloride intermediate has a longer half-life than had been believed (Gargas et al., 1986). This more stable intermediate may react with cellular nucleophiles such as reduced glutathione to yield $CO_2$, instead of spontaneously decomposing to CO (Figure 2).

In Pathway 2, glutathione transferase (GT) mediated the nucleophilic attack of $MeCl_2$ by reduced glutathione (GSH) (Anders et al., 1977; 1978a; Ahmed et al., 1980) (Fig. 2). The resulting S-chloromethyl glutathione rapidly hydrolyzed to yield S-hydroxymethyl glutathione, a hemimercaptal of formaldehyde and glutathione. Whether the S-hydroxymethyl glutathione hydrolyzed nonenzymatically to yield formaldehyde and regenerated GSH or ultimately yielded formic acid and GSH depended on the presence of formaldehyde dehydrogenase (FDH) and NAD+. FDH catalyzed the oxidation of S-hydroxymethyl glutathione to S-formyl glutathione. Further hydrolysis to form the products, formic acid and GSH, was catalyzed by S-formyl glutathione hydrolase. Formation of $CO_2$ occurred via oxidation of formaldehyde and formic acid (Elder, 1984).

Both pathways appeared to be dose-dependent in rats (McKenna and Zempel, 1981; McKenna et al., 1982). Further elucidation of the mechanisms of the series of reactions in these pathways and their kinetics has been reported (Kubic and Anders, 1978). Reviews of these mechanisms and their relation to the toxicity of $MeCl_2$ have been published (Ahmed et al., 1980; Andersen, 1981a; 1981b; Laib, 1982).

## SYNOPSIS OF $MeCl_2$ METABOLISM

The metabolism of $MeCl_2$ is enzyme-catalyzed and, therefore, has capacity-limited phenomena at high concentrations (Andersen, 1981a). First order kinetics are observed at low $MeCl_2$ concentrations and zero-order kinetics are observed at high concentrations.

The overall time course for $MeCl_2$ metabolism is complex due to contributions from at least 2 pathways with varying kinetic parameters (Andersen, 1981b). The CO-producing pathway (Pathway 1) appears to be a high affinity, low capacity pathway. The GSH-mediated pathway (Pathway 2) is a low affinity, high capacity first-order process at all accessible exposure concentrations (Gargas et al., 1986). The $V_{max}$ of $MeCl_2$ metabolism is thus a composite $V_{max}$ for the 2 pathways (Andersen, 1981b).

Because of the saturable character of $MeCl_2$ metabolism, the discrepancy between administered dose and effective dose becomes greater with increasing exposure doses. Therefore, extrapolations of potential toxicity of low doses based on data from high dose exposure and vice versa cannot be justified (McKenna and Zempel, 1981; McKenna et al., 1982).

In a review of the U.S. safety standards for occupational exposure to $MeCl_2$, it was reported that acute $MeCl_2$ toxicity was due to the formation of CO, and ultimately, COHb (Skrabalak and Babish, 1983). COHb concentrations greater than 10% produced headaches and dizziness, and those of 50 to 80%, produced unconsciousness, coma or death. Several factors influence $MeCl_2$ uptake, distribution, metabolism and excretion; these include smoking, level of physical exercise, and chronic pulmonary and cardiovascular problems (Skrabalak and Babish, 1983).

In addition, organ and species differences in the metabolic activation of $MeCl_2$ (Langenbach, 1984) and distribution differences due to vehicle and route of administration (Angelo et al., 1984) must be considered in the extrapolation of data from studies using animals to the safety assessment of $MeCl_2$ in humans. Several pharmacokinetic models have been proposed to clarify and predict the physiologic and biochemical behavior of $MeCl_2$ (Thomas, 1975; Withey and Collins, 1980; Andersen, 1981a; 1981b; McKenna and Zempel, 1981; McKenna et al., 1982; Angelo et al., 1984).

Several attempts have been made to determine a relationship between $MeCl_2$ toxicity due to CO formation and parameters of $MeCl_2$ metabolism such as substrate concentrations, metabolic rates and product concentrations (Peterson, 1978; McKenna et al., 1982; Andersen, 1981a).

## COVALENT BINDING OF $MeCl_2$ METABOLITE(S)

Covalent binding of radioactivity from $^{14}C$-$MeCl_2$ was observed in vivo in the livers of mice (Bergman, 1983) and in vitro in hepatic lipid and protein molecules of rats (Anders et al., 1977; Cunningham et al., 1981). No alkylation of DNA or RNA was observed in these studies (Cunningham et al., 1981) or in other studies in which DNA was isolated from the livers and salivary glands of rats and hamsters exposed to 3500 ppm $^{14}C$-$MeCl_2$ (Schumann, 1984) and from the livers and lungs of mice and rats exposed to 4000 ppm $^{14}C$-$MeCl_2$ (ICI, 1986b).

Both the formyl chloride intermediate of Pathway 1 and the S-chloromethyl glutathione intermediate of Pathway 2 (Fig. 2) were considered responsible for the observed covalent binding of radioactivity from $^{14}C$-$MeCl_2$ (Anders et al., 1977; 1978; Ahmed et al., 1980; Laib, 1982; Sipes and Gandolfi, 1980).

However, in vitro studies with hepatic microsomal fractions from rats treated with phenobarbital (P450 induction) or diethyl maleate (GSH depletion) indicated that S-chloromethyl glutathione may be the more reactive intermediate (Cunningham et al., 1981).

McKenna and Zempel (1981) suggested that the metabolic conversion of $MeCl_2$ to 1-carbon fragments provides appreciable potential for the incorporation of those fragments into a variety of endogenous substrates involved in normal intermediary and synthetic metabolism. No one yet has determined whether the "DNA alkylation by $MeCl_2$" actually represents true DNA adducts or incorporation of 1-carbon fragments into the macromolecule during synthesis of the nucleic acid bases. Sipes and Gandolfi (1980), using an in vitro system in which DNA synthesis would not be expected, did not detect significant incorporation of radioactivity from $^{14}C\text{-}MeCl_2$ into preformed DNA, a result which suggested that $MeCl_2$ does not alkylate DNA but was incorporated into the nucleic acid as part of a substrate during DNA synthesis. Incorporation of the 1-carbon fragments represented normal biochemistry and not DNA damage or a mutagenic event.

## COMPARISON WITH OTHER HALOGENATED HYDROCARBONS

Although the metabolism of $MeCl_2$ to CO is often compared to that of other dihalomethanes such as methylene bromide (Stevens et al., 1980) and bromochloromethane (Andersen, 198a), the magnitude and time course of CO formation vary among these compounds (Kubic et al., 1974; Kubic and Anders, 1975; Rodkey and Collison, 1977b; Gargas et al., 1986). Furthermore, "the 1- and 2-carbon haloalkanes, in contrast to haloalkenes, differ widely from each other regarding such properties as mechanisms of reactive metabolite formation and the chemical structure of their reactive metabolites" (Laib, 1982). Dihalomethanes are thought to use Pathway 2 (Fig. 2) in the formation of formaldehyde (Ahmed and Anders, 1976), although in vivo rate constants for $MeCl_2$, bromochloromethane, dibromomethane and difluoromethane vary in rats (Gargas et al., 1986).

## EXCRETION

### RATS AND MICE

Exposure of rats by inhalation to 50 to 1500 ppm $^{14}C$-$MeCl_2$ resulted in 5 to 55% of body burden dose-related excretion of $MeCl_2$ in expired air (McKenna et al., 1982). Exponential elimination of $MeCl_2$ was observed in the blood of rats after 4-hour inhalation exposure to 8000 and 52,000 mg/m$^3$ $MeCl_2$ (Maltseva, 1979) and in the urine of rats after 50 to 1500 ppm $^{14}C$-$MeCl_2$ inhalation exposures (McKenna et al., 1982). Urinary excretion of nonvolatile radioactivity after inhalation exposure to $^{14}C$-$MeCl_2$ ranged from 1% of doses from 412 to 930 mg/kg (DiVincenzo and Hamilton, 1975) to 8% of doses from 50 to 1500 ppm (McKenna et al., 1982).

After intraperitoneal injection of 412 to 930 mg/kg $^{14}C$-$MeCl_2$, 98% of the radioactivity was eliminated in the breath as $MeCl_2$ (91.5%), CO (2%), $CO_2$ (3%) and an uncharacterized metabolite (1.5%).

Although urinary excretion of nonvolatile metabolites was the primary elimination mode for inhaled $^{14}C$-$MeCl_2$ in rats and mice, some radioactivity was also detected in feces (McKenna et al., 1982; Bergman, 1983).

### DOGS

The concentrations of $MeCl_2$ excreted in the breath of dogs inhaling 100 to 200 ppm $MeCl_2$ were greater than that of humans. However, similar exponential respiratory excretion curves for humans and dogs were reported (DiVincenzo et al., 1972). Continuous inhalation of 5000 ppm $MeCl_2$ by dogs resulted in urinary excretion of 51 mg $MeCl_2$/l after 6 hours of exposure and 33 mg $MeCl_2$/l after 2 days of exposure. No change in urinary formic acid concentrations was observed (MacEwen et al., 1972).

HUMANS

Concentrations of exhaled $MeCl_2$ after inhalation of 50 to 500 ppm $MeCl_2$ by humans under various exposure conditions were proportional to the exposure concentrations. Repeated intermittent or continuous exposures for longer durations had very slight effects on the exhaled $MeCl_2$ concentrations (DiVincenzo et al., 1972; Stewart et al., 1976; Peterson, 1978; DiVincenzo and Kaplan, 1981a).

Post-exposure elimination by humans of inhaled $MeCl_2$ was less than 5% of the 70% $MeCl_2$ absorbed (DiVincenzo and Kaplan, 1981a) indicating the major role of biotransformation in the elimination of $MeCl_2$.

Respiratory excretion of $MeCl_2$ by humans after inhalation of 50 to 200 ppm $MeCl_2$ decreased exponentially to < 0.1 to 1 ppm in 4 to 16 hours (DiVincenzo et al., 1972; DiVincenzo and Kaplan, 1981a; 1981b). Four phases in respiratory excretion were observed from less than 2 minutes to 1 hour following exposure (Riley et al., 1972).

Increased physical exercise during exposure had no effect on respiratory elimination of $MeCl_2$ (DiVincenzo and Kaplan, 1981b). During exposure, smoking increased exhaled $MeCl_2$ concentrations; however, post-exposure exponential respiratory elimination curves were similar for smokers and control non-smokers (DiVincenzo and Kaplan, 1981b).

Respiratory excretion of $MeCl_2$ was measured in humans following immersion of thumbs in liquid $MeCl_2$ for 30 minutes (Stewart and Dodd, 1964). A maximum mean concentration of 3.1 ppm $MeCl_2$ was detected in exhaled air. Following exposure, a rapid exponential decline in expired $MeCl_2$ concentrations to less than 0.1 ppm was observed within 5 hours.

Urinary excretion of $MeCl_2$ was related to exposure concentrations. Average excretion after exposure for 2 hr to 100 ppm $MeCl_2$ by inhalation was 22.6 µg over 24 hr, and after exposure to 200 ppm for 2 hr, 81.5 µg $MeCl_2$ over 24 hr (DiVincenzo et al., 1972). Urinary excretion rates of 142 to 318 µg/day of $MeCl_2$ and 138 to 242 µg/day of $MeCl_2$ were not affected by intensity of physical exercise or by smoking, respectively (DiVincenzo and Kaplan, 1981b). Neither smoking nor physical exercise affected urinary concentrations of chloride ion, formaldehyde, and formic acid (DiVincenzo and Kaplan, 1981b).

## ANIMAL TOXICOLOGY

### ORAL STUDIES

### ACUTE TOXICITY

Single doses of $MeCl_2$ have been administered to rats (Cignoli and Castro, 1971; Johnson, 1965; Kimura et al., 1971; Laham et al., 1978; Moody et al., 1981; Reynolds, 1972; Reynolds and Yee, 1967; 1968; Sasame et al., 1968; Ugazio et al., 1973), mice (EPA, 1985a; Matsumoto et al., 1982; Zakhari, 1977), and dogs (Barsoum and Saad, 1934) (Table 4). The LD50 value for $MeCl_2$ administered orally to adult rats ranged from 1.06 to 2.3 ml/kg. In the Hodge and Sterner (1949) classification of single-dose oral toxicity for rats, $MeCl_2$ would be classified as slightly toxic.

TABLE 4

ACUTE ORAL STUDIES

| Material Tested | Method | Species of Animal | LD50 | Results and Comments | References |
|---|---|---|---|---|---|
| $MeCl_2$, unspecified vehicle | 2 rats were dosed by stomach tube with 11 mmol/kg $MeCl_2$ in a 0.2 ml volume and were killed 2 hr later. | Female rats; unspecified strain | - - - | Hepatic glutathione concentration as a percentage of the mean concentration in 10 control rats was 106 percent and 99 percent in 2 treated rats, respectively. | Johnson, 1965 |
| $MeCl_2$, undiluted | Groups of 6 to 12 male and female newborn rats (24 to 48 hr old and 5 to 8 g) and immature 14 day old rats (16 to 50 g) and groups of 6 male young adult rats (80 to to 160 g) and older adult rats (300 to 470 g) were intubated and were observed for 1 week. | Newborn rats,<br>Immature rats,<br>Young adult rats,<br>Older adult rats;<br>Sprague-Dawley strain | < 1.0 ml/kg<br>1.8 ml/kg<br>1.6 ml/kg<br>2.3 ml/kg | The LD50 could not be more accurately determined in the newborn rats due to volume limitations.<br>Gross signs of $MeCl_2$ action were first observed in young adult rats after a dose of 1 ml/kg. | Kimura et al., 1971 |
| $MeCl_2$ | Oral administration. | Male rats,<br>Female rats;<br>Sprague-Dawley strain | 1.72 ml/kg<br>1.06 ml/kg | Oral doses greater than 0.4 ml/kg produced vascular changes accompanied by central nervous system depression and gastrointestinal hemorrhage. | Laham et al., 1978 |
| $MeCl_2$, in mineral oil | 1000 mg/kg $MeCl_2$ was administered by gastric intubation in a volume of 5.0 ml/kg to groups of 3 rats. The rats were killed 1 or 18 hr later and liver microsomal extracts were prepared. | Male rats; Sprague-Dawley strain | - - - | The liver diene conjugate concentration was significantly less in the treated rats killed at 1 hr than in the control rats. The rats killed at 18 hr had a greater loss of body weight than the control rats. There was 100 percent survival to 18 hr. The liver-to-body weight ratio and microsomal protein, RNA, and phospholipid concentrations were not significantly different from the control values. The liver microsomal cytochrome P-450 and stearic acid concentrations were significantly decreased. NADPH cytochrome c reductase, cytochrome $b_5$, and the palmitic, oleic, linoleic, arachidonic, and docosahexanoic acid concentrations were not significantly different from control values. The researchers concluded that microsomal lipid peroxidation was not observed. | Moody et al., 1981 |
| $MeCl_2$, in mineral oil | 4 rats given 2600 μmol/100 g body weight of $MeCl_2$ by stomach tube. 25 control rats received 0.5 ml mineral oil or saline. Rats killed two hr later; 30 min prior to death, given radioactive glycine intraperitoneally. Liver microsomal extracts prepared. | Male rats; unspecified strain | - - - | The RNA content of the cell sap, glycine incorporated, and microsomal protein and lipid conjugated diene contents and the activities of oxidative demethylase, glucose-6-phosphatase and NADPH-tetrazolium reductase were not significantly different from control values. No | Reynolds, 1972 |

TABLE 4 - Continued

ACUTE ORAL STUDIES

| Material Tested | Method | Species of Animal | LD50 | Results and Comments | References |
|---|---|---|---|---|---|
| MeCl$_2$, in mineral oil (continued) | | | | necrosis was observed. In several similar experiments investigating hepatocyte injury, MeCl$_2$ had very little effect on the enzyme activities and parameters measured (Reynolds and Yee, 1967; 1968). | |
| MeCl$_2$ | Rats (unspecified number) killed 3 to 4 hr after oral MeCl$_2$ administration. | Rats | - - - | Liver glucose-6-phosphatase activity was not decreased. | Cignoli and Castro, 1971 |
| MeCl$_2$ | 5 rats fasted 12 hr, then given 1.25 ml/kg MeCl$_2$ orally, and then killed 3 hr later. Liver microsomal extracts prepared. | Male rats; Sprague-Dawley strain | - - - | At doses greater than 1.25 ml/kg, some of the rats died. There was no significant change from control values in the cytochrome P-450 content. There was a small but not significant increase in the N-demethylation of ethylmorphine. | Sasame et al., 1968 |
| MeCl$_2$ | Oral administration to rats (unspecified number) of doses of 1.29 mmol/100 g body weight of MeCl$_2$ and greater. Control rats treated with mineral oil. | Male albino rats; Wistar strain | - - - | The serum aspartate aminotransferase activity 24 hr after dosing with 1.29 mmole/100 g body weight MeCl$_2$ was not different from the control value. The LD95 was 5.16 mmol/100 g body weight; last death observed at 24 hr. Death attributed to anaesthetic rather than metabolic effects. | Ugazio et al., 1973 |
| MeCl$_2$ | Oral administration | Mice; unspecified strain | 1987 mg/kg | - - - - | EPA, 1985; Zakhari, 1977 |
| MeCl$_2$, in olive oil | Oral administration of MeCl$_2$ in a 0.2 ml volume to mice (unspecified number) followed by examination of brain, cerebellum, lung, stomach, intestine, liver, and kidney. | Male mice; ddY strain | 4.77 g/kg | Peeling of the mucous membrane and bleeding were observed in stomach and intestines. 24 hr after oral doses of 0.238 and 0.477 g/kg MeCl$_2$, no changes in activities of glutamic-oxaloacetic transaminase and glutamic-pyruvic transaminase. | Matsumoto et al., 1982 |
| MeCl$_2$, emulsified with 3 times its volume of mucilage of acacia | 7 dogs were anesthetized and their stomachs were lavaged, then 2.0 to 5.0 g/kg MeCl$_2$ (10.0 to 31.2 g total dose) was administered by stomach tube. All animals were observed for at least 24 hr. | Dogs | - - - | Minimum lethal dose of MeCl$_2$ was 3.0 g/kg and all deaths occurred within 24 hr. Deaths attributed to respiratory arrest. | Barsoum and Saad, 1934 |

## SHORT-TERM TOXICITY

$MeCl_2$ was dissolved in corn oil and administered by gavage in a total volume of 0.2 ml/30 g body weight daily for 14 consecutive days to male CD-1 mice (Condie et al., 1983). The mice were killed on day 14, the livers and kidneys were examined, and selected biochemical and clinical chemistry tests were performed. Four groups of at least 8 mice each received 0, 133.0, 333.0, and 665.0 mg/kg $MeCl_2$, respectively. $MeCl_2$ did not significantly affect the body weights of the mice. p-Aminohippurate uptake by kidney cortical slices was significantly inhibited by all $MeCl_2$ doses; measurement of the active uptake of the organic acid, p-aminohippurate, by kidney cortical slices serves as an indication of the functioning of the renal proximal tubules. Blood urea nitrogen and serum creatinine concentrations were also used to evaluate renal function; these and serum glutamate-pyruvate transaminase were not affected by $MeCl_2$. The liver and kidneys from 5 mice from each group were examined. $MeCl_2$ caused a treatment-related increase in the incidence of tubular epithelial hyperplasia and mesangial hypertrophy in the kidneys and mitotic figures and cytoplasmic vacuolization in the liver; changes were minimal to slight in severity. The only significant histologic change related to $MeCl_2$ administration was minimal to slight hepatic centrilobular cytoplasmic vacuolization.

## SUBCHRONIC TOXICITY

$MeCl_2$ was administered in the drinking water at a concentration of 125 mg/l to rats for 13 weeks (Bornman and Loeser, 1967; World Health Organization [WHO], 1984). No effects were observed on behavior, body weights, hematology, urinalyses, blood glucose, plasma-free fatty acids, and estrus cycles.

Groups of 20 Fischer 344 rats of each sex were given 0.15, 0.45, and 1.50% $MeCl_2$ in drinking water for 90 days (Kirschman et al., 1986). Consumption of $MeCl_2$ was calculated as 166, 420, and 1200 mg/kg/day for males and 209, 607, and 1469 mg/kg/day for females. Slightly decreased bpdu weights were observed in mid-dose males and high dose females throughout the study. Water consumption decreased with $MeCl_2$ concentration. Treated and control animals were not different in regard to mortality, physical observations, food consumption, feed effiency, and gross necropsy results. There were no $MeCl_2$-related effects observed at histopathological evaluation of tissues from rats from the 1 month interim necropsies. However, there were hepatocellular changes at 3 months; central lobular necrosis and granulomatous foci and ceroid or lipofuscin accumulation and cytoplasmic eosinophilic bodies were observed in high dose rats and some mid-dose females. A dose-dependent increased incidence of hepatocyte vacuolation was also observed; many of these vacuoles contained lipid, generalized or concentrated in the central lobular region.

Groups of 20 $B6C3F_1$ mice of each sex were given 0.15, 0.45, and 1.50% $MeCl_2$ in drinking water for 90 days (Kirschman et al., 1986). Consumption of $MeCl_2$ was 226, 587, and 1911 mg/kg/day for males and 231, 586, and 2030 mg/kg/day for females.

Slightly lower body weights were observed in mid-dose and high dose mice from week 6 to the end of the study. Water consumption decreased in treated animals. Treated and control mice were not different in regard to physical observations, opthalmology, and food consumption. There were no $MeCl_2$-related effects observed at histopathological evaluation of tissues from mice from the 1 month interim necropsies. However, there were subtle central lobular fatty changes in livers, most prominent in mid-dose and high dose mice, at 3 months. There were no other $MeCl_2$-related changes.

Additional subchronic and chronic oral experiments with rats are described in the section on teratogenicity (Bornmann and Loeser, 1967; Clayton and Clayton, 1981; Nishio et al., 1984; WHO, 1984). A chronic study with rats fed coffee decaffeinated with $MeCl_2$ is described in the section on carcinogenicity (Wurzner et al., 1977).

## DERMAL STUDIES

### ACUTE TOXICITY

The abdominal skin of groups of 10 rats (unspecified strain) was shaved, and 3 days later, the rats were intubated with 40 ml/kg of water, and an inverted beaker containing 2 ml of liquid $MeCl_2$ was placed on the shaved area for 2, 5, 10, 15, or 20 min (NIOSH, 1976; Schutz, 1958; 1960). After $MeCl_2$ exposure, the skin was blotted dry, and urine was collected for the following 3 hr. As exposure time increased, the volume of urine voided in 3 hr decreased; controls (unspecified number) and rats exposed for 2 min voided 8 ml, and rats exposed for 20 min voided less than 1.0 ml. Hemoglobin was observed in the urine of 5, 8, 9, 7, and 5 rats of 10 rats each in the groups exposed to $MeCl_2$ for 2, 5, 10, 15, and 20 min, respectively. No hemoglobin was observed in the urine of control rats.

### PRIMARY SKIN IRRITATION

$MeCl_2$ was a severe primary skin irritant for New Zealand female rabbits (Duprat et al., 1976; National Library of Medicine [NLM], 1985). Six rabbits were patch tested with 810 mg $MeCl_2$ for 24 hours by the Draize method (Draize et al., 1944). The mean Draize score for primary skin irritation was 5.2 of a possible total of 8.0.

$MeCl_2$ was mildly irritating to the skin of rabbits on repeated contact when allowed to evaporate (Clayton and Clayton, 1981).

Cotton was soaked in $MeCl_2$ and applied for 1 minute to the ears of rabbits (unspecified number) once a day, 5 days a week for 4 weeks (Heppel et al., 1944). Mild simple irritation was observed. The fat solvent action of $MeCl_2$ made the hair follicles appear more prominent. Hyperemia was followed by a scaly exfoliation.

## OCULAR STUDIES

$MeCl_2$ was a moderate eye irritant for New Zealand female rabbits (Duprat et al., 1976; NLM, 1985). The Draize method was used and doses of 162 mg $MeCl_2$ were instilled into the eyes of 6 rabbits (Draize, 1944). The mean Draize score for ocular lesions was 33.0 of a possible total of 110.0.

A 0.1 ml dose of $MeCl_2$ was instilled into the conjunctival sac of the right eye of 30 female New Zealand rabbits and the eyelids were held together for a few seconds; 6 animals were used for eye irritation studies, 6 for _in vivo_ measurement of corneal thickness, 6 for measurement of intraocular tension, and 12 for histopathologic studies (Ballantyne et al., 1976). A 0.01 ml dose of $MeCl_2$ was instilled into the eyes of 18 rabbits; 6 rabbits were used for eye irritation studies, 6 for measurement of corneal thickness, and 6 for measurement of intraocular tension. A 0.02 ml dose of $MeCl_2$ was instilled into the eyes of 6 rabbits and intraocular tensions were measured. Two groups of 15 rabbits were exposed for 10 minutes to 1,750 and 17,500 $mg/m^3$ $MeCl_2$ vapor concentrations; in each group, 3 rabbits were examined for eye irritation, 6 rabbits were used for measurement of corneal thickness, and 6 for measurement of intraocular tension. Eye irritation was assessed at

10 minutes; 1, 6, and 24 hours; and then daily for 2 weeks following exposure to $MeCl_2$. Corneal thickness was measured in vivo using an optical depth measuring device before $MeCl_2$ exposure and at 30 minutes, 1 and 6 hours, and then daily for 11 days following exposure to $MeCl_2$. Intraocular tension was measured with a Draeger hand-held applanation tonometer before exposure to $MeCl_2$ and at 10 minutes; 1, 5, and 24 hours; and then daily after $MeCl_2$ exposure until tensions returned to normal. For the histopathologic studies, rabbits were killed 6 hours and 1, 2, 4, 7, and 14 days after exposure to $MeCl_2$, and the globes were removed. The instillation of 0.1 ml $MeCl_2$ into the conjunctival sac of rabbits caused moderate inflammation of the conjunctiva and eyelids and corneal injury. Excess lacrimation and chemosis lasted for about a week and vascular injection of the conjunctiva and lid margins for almost 2 weeks. Iritis, lasting from 1 to 7 days, and just detectable to marked keratitis, accompanied by corneal neovascularization, were observed in two-thirds of the rabbits. Corneal injury was confirmed by measurements of corneal thickness and histopathological examination. The mean peak increase in corneal thickness occurred at 6 hours and thickness did not return to normal for 8 or 9 days. Histopathological findings included edema, congestion, neutrophil infiltration, goblet cell proliferation and epithelial detachment of the conjunctiva, with neutrophil infiltration and denudation of the corneal epithelium. However, healing did occur, as indicated by macroscopic and histological observations. Inflammatory lesions of conjunctiva and eyelid were as marked but were less persistent after the instillation of 0.01 ml $MeCl_2$ into the conjunctival sac of rabbits than after 0.1 ml $MeCl_2$. Minor and transient corneal injury was observed in a

small number of rabbits. Mean maximum increase in corneal thickness was less but not proportionately less than occurred with 0.1 ml $MeCl_2$. Following exposure to $MeCl_2$ vapor, eye irritation was not observed. Small increases in corneal thickness related to the degree of exposure were observed. Both instillation of $MeCl_2$ into the conjunctival sac of rabbit and exposure of rabbits to $MeCl_2$ vapor caused an increase in intraocular tension. The rise in tension seemed to be dose- or degree of exposure-related.

## INHALATION STUDIES

### ACUTE TOXICITY

$MeCl_2$ has been studied in acute inhalation studies with rats (Capel and Williams, 1978; Clark and Tinston, 1982; Fodor and Winneke, 1971; Heppel et al., 1944; Imperial Chemical Industries [ICI], 1986a; 1986b; Kurppa et al., 1981; National Toxicology Program [NTP], 1986), mice (Alexeeff and Kilgore, 1983; Aviado, 1975; 1977; Gehring, 1968; Heppel et al., 1944; ICI, 1986a; 1986b; Kjellstrand et al., 1985; NTP, 1986; Svirbely et al., 1947), guinea pigs (Balmer et al., 1976; Heppel et al., 1944; Morris and Smith, 1976; Morris et al., 1979), rabbits (Heppel et al., 1944; Taylor et al., 1976), dogs (Adams and Erickson, 1976; Aviado, 1977; 1978; von Oettingen et al., 1949), and monkeys (Aviado, 1975; Belej et al., 1974) (Table 5).

### SUBCHRONIC AND CHRONIC TOXICITY

$MeCl_2$ has been studied in subchronic and chronic inhalation studies with rats (Fuxe et al., 1948; Haun et al., 1977; Heppel et al., 1944; Heppel and Neal, 1944; ICI, 1986a; Kurppa and Vainio, 1981; Leuschner et al., 1984; MacEwen et al., 1972; NTP, 1986; Norpoth et al., 1974; Sahu and Lowther, 1981;

TABLE 5

ACUTE INHALATION STUDIES

| $MeCl_2$ Concentration | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 0.1 ml/l | 2.4 ml of $MeCl_2$ placed in a 24 l chamber and vapor distributed with a fan. Rats exposed 5 times at 1 hr intervals for 5 min 24 hr later, the rats were killed, and liver, lungs, and kidneys removed and and homogenated and enzyme activities determined. | 9 male Sprague-Dawley treated rats and 9 control rats | Hepatic, renal, and pulmonary uridine diphosphoglucuronic acid transferase activities were unchanged. Hepatic microsomal cytochrome P-450, hepatic, renal and pulmonary lysosomal β-glucuronidase and kidney microsomal β-glucuronidase activities were decreased. Hepatic and pulmonary microsomal β-glucuronidase were increased. | Capel and Williams, 1978 |
| - - - | For LC50 study, rats were exposed to $MeCl_2$ for 5 min and deaths were recorded. For CNS study, rats were exposed to $MeCl_2$ for 10 min. | Groups of 6 male or 6 female Alderly Park rats | The LC50 was 5.7 percent $MeCl_2$. The concentration of $MeCl_2$ that caused CNS depression in 50 percent of the rats was 0.9 percent. Rats that died progressed from slight ataxia to loss of righting reflex to loss of movement to narcosis to shallow respiration and to death from respiratory depression. | Clark and Tinston, 1982 |
| 1000 ppm (34 mg/l) | Rats were exposed to $MeCl_2$ for 7 hr and were observed for one month. | 10 rats | No rats died. | Fodor and Winneke, 1971 |
| 500, 1000, and 5000 ppm | Rats were exposed to $MeCl_2$ for 24 hr and sleep-wakefulness-behavior was assessed with electroencephalograms (EEGs) and electromyograms (EMGs). | Female albino Ivan-Wistar rats, probably groups of 5 | Sleep time was increased, but not significantly, rapid eye movement (REM) sleep was decreased significantly, and the time between successive REM-periods was significantly increased following exposure to 1000 and 5000 ppm $MeCl_2$. The effects following exposure to 500 ppm $MeCl_2$ were in the expected direction but were less pronounced. The researchers stated that these results were an indication of central nervous system disturbances. | Heppel et al., 1944 |
| 1000 ppm | Rats were exposed to $MeCl_2$ for 3 hr. The rats were killed, microsomes were prepared from renal and hepatic samples, and enzymes activities were determined. | 5 male Wistar treated rats and 5 controls | Renal microsomal ethoxycourmain O-deethylase activity increased in exposed rats. No change was observed in renal microsomal cytochrome P-450 activity, or in hepatic microsomal NADPH cytochrome c-reductase, cytochrome P-450, ethoxycoumarin O-deethylase, and ethoxyresorufin O-deethylase activities. | Kurppa et al., 1981 |
| 2000 and 4000 ppm | Rats were exposed to $MeCl_2$ for 6 hr and were killed the next day. Lungs and liver were examined. | Groups of 10 male Fischer 344 rats and 10 controls | $MeCl_2$ had a mild anaesthetic effect. No abnormalities were observed. | ICI, 1986a |
| 4000 ppm (radioactive) | All rats were exposed for 3 hr and 4 rats were killed at 6, 12, and 24 hr, respectively after initial exposure. Livers and lungs removed and $MeCl_2$ binding to DNA and protein measured. | 12 male Fischer 344 rats rats and controls | Low concentrations of radioactivity found in pulmonary and hepatic DNA and protein. There was no evidence for alkylation of DNA by $MeCl_2$. | ICI, 1986b |
| 15500, 16500, 16800, 17250, 18500, and 19000 ppm $MeCl_2$ | Rats were exposed for 4 hr and were observed for 14 days. Necropsies were performed on all rats. | Groups of 5 male and 5 female F344/N rats exposed to up to 18500 ppm $MeCl_2$. Three groups exposed to 19000 ppm $MeCl_2$. No controls. | Survival ranged from 2 to 5 of 5 rats. No compound related effects were observed at necropsy. | NTP, 1986 |

TABLE 5 - Continued

ACUTE INHALATION STUDIES

| $MeCl_2$ Concentration | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 160 mg/l | Mice were tested in a passive-avoidance conditioning experiment that consisted of a training trial and a test for recall 1 to 4 days later. The mice were exposed to $MeCl_2$ until loss of the righting reflex, usually for 20 sec, 1 hr prior to the training trial. A hot-plate technique was used to test the analgesic potential of $MeCl_2$ for 3 wk old mice. | 15 to 41 3-wk old, 15 to 45 5-wk old, and 15 to 75 8-wk old treated male Swiss-Webster mice. 20 to 101 control mice of each age group. | Exposed mice not different from control mice in training trial latencies. Treated mice recovered from obvious effects of excitation and narcosis in 5 to 10 min. $MeCl_2$ exposure impaired passive-avoidance learning particularly at 1 or 2 days following training. Younger mice exhibited the most impairment in learning. In the analgesia test, treated and control mice did not react differently. $MeCl_2$ caused a decrease in weight gain in only the 8-wk old mice. | Alexeeff and Kilgore, 1983 |
| 40 percent | Cardiac arrythmia induced by $MeCl_2$ scored on an intensity of response scale of + to +++. | Mice, unspecified strain | Cardiac arrythmia induced by a minimum concentration of 40 percent $MeCl_2$ was a + response. | Aviado, 1975; 1977 |
| 13500 ppm | Mice were exposed to $MeCl_2$ for 50 to 800 min (estimated from figure) and 24 hr later the mice were anesthetized with methoxyflurane, blood was sampled, and the SGPT was determined. | Groups of 5 to 40 female female Swiss-Webster mice. 254 control mice. | The time of death for one-half the mice was 640 min. The time to onset of anesthesia for one-half the mice was 128 min. The time to elevation of SGPT for one-half the surviving mice was 730 min. | Gehring, 1968 |
| 10000 ppm (34 mg/l) | Mice were exposed to $MeCl_2$ for 4 hr. | 16 mice, unspecified strain | One mouse died. | Heppel et al., 1944 |
| 400, 550, 600, 750, 850, 1100, 2200, and 2500 ppm | A Doppler radar unit was used to measure motor activity counts of mice exposed for 1 hr to $MeCl_2$. | Groups of 13 male NMRI mice at $MeCl_2 \geq 850$ ppm and groups of 24 at $MeCl_2 \leq 750$ ppm | No effects were observed on motor activity at 600 ppm $MeCl_2$ and below. At higher concentrations, $MeCl_2$ had a biphasic effect on motor activity; it at first increased, then decreased at the end of exposure, reached a minimum 1 to 2 hr after exposure, and then returned to normal. | Kjellstand et al., 1985 |
| 15900, 16500, 16800, 17250, 18500, and 19000 ppm $MeCl_2$ | Mice were exposed for 4 hr and were observed for 14 days. Necropsies were performed on all mice. | Groups of 5 male and 5 female B6C3F$_1$ mice exposed to up to 18500 ppm $MeCl_2$. Three groups exposed to 19300 ppm $MeCl_2$. No controls. | The LC50 for male mice was calculated as 17703 ppm $MeCl_2$. No meaningful LC50 could be calculated for female mice; survival ranged from 2 to 5 of 5 rats. No $MeCl_2$-related effects were observed at necropsy. | NTP, 1986 |
| 39.9 to 58.7 mg/l | Mice were exposed to $MeCl_2$ for 7 hr and the number of fatalities within 2 weeks were recorded. | Groups of 20 white Swiss mice | The LC50 for $MeCl_2$, calculated 24 hr after the end of exposure, was 56.23 mg/l (16180.6 ppm). Most of the mice died 24 hr after the end of exposure; some died 48 hr later. Mice exposed to $MeCl_2$ were restless, had muscular twitchings, uncoordinated movements, and labored respiration, and developed narcosis. | Svirbely et al., 1947 |
| 2000 and 4000 ppm | Mice were exposed to $MeCl_2$ for 6 hr and were killed the next day. Lungs and livers were examined. | Groups of 10 male B6C3F1 mice and 10 controls | $MeCl_2$ had a mild anaesthetic effect. A highly selective vacuolation and pyknosis of non-ciliated (clara) cells of the bronchidar epithelium was observed. Pale enlarged mitochondria were observed in pulmonary cells. There was an increase in myelin whorls in the bile canaliculi of the centrilobular hepatocytes in the 4000 ppm group. | ICI, 1986a |

TABLE 5 - Continued

ACUTE INHALATION STUDIES

| $MeCl_2$ Concentration | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 4000 ppm (radioactive) | All mice were exposed for 3 hr and 20 mice were killed at 6, 12, and 24 hr, respectively after initial exposure. Additional 39 mice were exposed for 3 hr and killed 6 hr after initial exposure. Livers and lungs removed and $MeCl_2$ binding to DNA and protein measured. | 60 male B6C3F1 mice and controls; 39 additional male B6C3F1 mice | Low concentrations of radioactivity found in pulmonary and hepatic DNA and protein (mouse DNA contained more radioactivity than rat DNA). There was no evidence of alkylation of DNA by $MeCl_2$. | ICI, 1986b |
| 5000 to 16000 ppm | Guinea pigs were exposed to $MeCl_2$ for 6 hr and deaths were recorded during exposure and for 18 hr afterwards. | 5 to 20 male Hartley guinea pigs per group | The 6 hr LC50 was 11600 ppm $MeCl_2$. | Balmer et al., 1976 |
| 10000 ppm (34 mg/l) | Guinea pigs were exposed to $MeCl_2$ for 7 hr and were observed for one month. | 9 guinea pigs | No guinea pigs died. | Heppel et. al., 1944 |
| 4500 to 5000 ppm range | Guinea pigs were exposed to $MeCl_2$ for 6 hr and were killed with an overdose of pentobarbital. Blood was sampled. Histologic examination of and biochemical tests were performed on the liver. | Groups of 5 to 35 male Hartley treated guinea pigs and controls | Fatty liver was induced by $MeCl_2$. $MeCl_2$ increased hepatic triglyceride but did not affect serum free fatty acid concentration or the incorporation of palmitic acid into triglyceride by liver slices. Serum triglyceride was reduced. Hepatic protein synthesis was normal. The researchers suggested that $MeCl_2$ caused the depletion or alteration of some serum component necessary for normal hepatic triglyceride secretion. | Morris and Smith, 1976<br>Morris et al., 1979 |
| 10000 ppm (34 mg/l) | Rabbits were exposed to $MeCl_2$ for 7 hr and were observed for one month. | 4 rabbits | One rabbit died several days after exposure. | Heppel et al., 1944 |
| 5 percent | Rabbits were anesthetized with sodium pentobarbital and an endotracheal tube was placed surgically. $MeCl_2$ was delivered to the trachea. Blood was sampled and cardiovascular measurements were made before and 1 min after exposure to $MeCl_2$. | 6 treated male New Zealand white rabbits | Rate of change of left ventricle pressure, cardiac output, and stroke volume were significantly decreased. Mean arterial, left ventricular systolic, left ventricular end-diastolic, and central venous pressure, and cardiac rate were not different following $MeCl_2$ exposure. Peripheral vascular resistance was increased. | Taylor et al., 1976 |

TABLE 5 - Continued

ACUTE INHALATION STUDIES

| $MeCl_2$ Concentration | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 500, 1000, 2000, and 5000 ppm | Dogs exposured to 2 hr of $MeCl_2$ at 2 to 3 day intervals. $MeCl_2$ introduced via a permanent tracheostomy. Heart instrumented with a blood flow transducer and a pressure transducer. Arterial pressure measured and blood samples taken at 30 min intervals. | 8 mongrel dogs | Coronary blood flow increased above control by 1000, 2000, and 5000 ppm $MeCl_2$. Myocardial contractility and arterial pressure increased. No change in heart rate. Respiration and body temperature decreased. CNS depression observed. $MeCl_2$ was arrythmogenic in 4 dogs. Atrioventricular blocks, preventicular contractions, and paroxysmal ventricular tachycardia observed. Heart was permanently damaged. Hemoglobin and hematocrit decreased. Heinz bodies observed on blood smears. Red blood cells had crenated margins and were irregularly contracted. Increased osmotic fragility observed. Hemosiderin observed in the liver and spleen. Erythrocytic glucose-6-phosphate dehydrogenase activity decreased. The researchers suggested that $MeCl_2$ induced hemolytic anemia. | Adams and Erickson, 1976 |
| 2.5 percent | Dogs anesthetized and exposed to $MeCl_2$. | Dogs | Myocardial contractivity depressed by a minimum concentration of 2.5 percent $MeCl_2$. | Aviado, 1977 |
| 5 percent | Dogs anesthetized wtih pentobarbital and artificially ventilated. Hearts instrumented. Exposed to $MeCl_2$ for 5 minutes. | 10 mongrel dogs | Myocardial contractility was depressed. No significant changes observed in arterial blood pressure, heart rate, coronary blood flow, or vascular resistance (except that mean coronary vascular resistance was signficantly increased in one group of 5 dogs). | Aviado, 1978 |
| 15000 ppm | Dogs were exposed to $MeCl_2$ for 7 hr. | 4 dogs | Arterial and venous blood pressure and respiratory rate increased at the beginning of exposure and then decreased during exposure. Heart rate also decreased. Corneal and pupillary reflexes were absent within the first 26 min of exposure. The dogs had frequent tremors, walking movements, twitching, and rythmic contractions of the diaphragm. Body temperature fell at first and then increased. | von Oettingen et al., 1949 |

TABLE 5 - Continued

ACUTE INHALATION STUDIES

| $MeCl_2$ Concentration | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 20000 ppm | Dogs were exposed to $MeCl_2$ for up to 7 hr. | 3 dogs | One dog died after 315 minutes; the other 2 were killed at the end of the experiment. Blood pressure increased at the beginning of exposure and then it and heart rate decreased. Respiratory rate increased initially and then decreased. Corneal and pupillary reflexes were absent at 22 min. Convulsive movements, rythmic walking movements, and twitchings were observed. Body temperature decreased. | von Oettingen, 1949 |
| 40000 ppm | Dogs were exposed to $MeCl_2$ for up to 4 hr. | 5 dogs | All 5 dogs died during the experiment; the earliest died at 1.5 hr and the latest at 4 hr. Blood pressure increased at the beginning of exposure and then it fell rapidly and venous pressure increased until death. Heart rate also increased and then fell. Respiration decreased initally, then increased, and then decreased again. The heart stopped prior to respiratory arrest. Tremors, twitchings, and convulsive movements were observed during exposure initially. Corneal and pupillary reflexes were absent at 8 min and complete muscular relaxation or narcosis was observed at about 16 min. Body temperature decreased. | von Oettingen et al., 194 |
| 2.5 and 5.0 percent | Monkeys anesthetized with sodium pentobarbital, artificially ventilated and exposed to $MeCl_2$.<br>Cardiac arrythmia, tachycardia in anesthetized monkeys, open-chest myocardial depression and closed-chest hypotension induced by 5.0 percent + $MeCl_2$ scored on an intensity of response scale of + to +++. Unspecified concentration of $MeCl_2$ tested for early respiratory depression. | Groups of 3 rhesus monkeys for cardiotoxicity study. Unspecified number for respiration study. | Cardiac arrythmia, tachycardia, myocardial depression, and hypotension induced by a minimum concentration of 5.0 percent $MeCl_2$ were + responses. Only aortic blood pressure increased at 2.5 percent $MeCl_2$. $MeCl_2$ did not cause respiratory depression. | Aviado, 1975; Belej et al., 1974 |

Sahu and Ulsamer, 1980; Sahu et al., 1980; Savolainen et al., 1977; Toftgard et al., 1982), mice (Haun et al., 1971; ICI, 1986a; MacEwen et al., 1972; NTP, 1986; Thomas et al., 1971; Weinstein et al., 1971; 1972), guinea pigs (Balmer et al., 1976; Heppel et al., 1944), gerbils (Rogengren et al., 1986), rabbits (Heppel et al., 1944), cats (Heppel et al., 1944), dogs and pups (Haun et al., 1971; Heppel et al., 1944; Leuschner et al., 1984; MacEwen et al., 1972), and monkeys (Haun et al., 1971; Heppel et al., 1944; MacEwen et al, 1972) (Table 6).

A deodorant formulation containing $MeCl_2$ has also been studied in a subchronic inhalation study with monkeys (Meltzer et al., 1977) (Table 8).

Additional subchronic $MeCl_2$ inhalation studies with rats (Bornschein et al., 1980; Hardin and Manson, 1980) and with rats and mice (Leong et al., 1975; Schwetz et al., 1975) are described in the section on teratogenicity, and additional chronic $MeCl_2$ inhalation studies with rats and hamsters (Burek et al., 1979; Rampy et al., 1979; Reznik, 1984)~~,~~ and chronic inhalation studies with rats and mice (NTP, 1986) are described in the section on carcinogenicity.

## INTRAPERITONEAL STUDIES

Single intraperitoneal doses of $MeCl_2$ have been administered to rats (Cornish et al., 1973; Corsi et al., 1983; Hamada and Peterson, 1977; Harms et al., 1976; Kluwe et al., 1982; Pankow et al., 1979; Sagai and Tappel, 1979), mice (Juorio and Yu, 1985; Klaassen and Plaa, 1966; Plaa and Larson, 1965), guinea pigs (DiVincenzo and Krasavage, 1974), and dogs (Klaassen and Plaa, 1967) (Table 7). The LD50 value for $MeCl_2$ administered intraperitoneally to male mice was 1.5 ml/kg (23 mmol/kg), and the LD50 value for female mongrel dogs was 0.95 ml/kg (15 mmol/kg).

An additional intraperitoneal study in mice is described in the section on carcinogenicity (Theiss et al., 1977).

TABLE 6

SUBCHRONIC AND CHRONIC INHALATION STUDIES

| Material and Concentration Tested | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 70, 300, and 1000 ppm $MeCl_2$ | Rats exposed 6 hr per day for 3 days and killed 16 to 18 hr later. Biochemical tests performed on serum and brain. | Groups of 6 male Sprague-Dawley rats | $MeCl_2$ produced a selective reduction in dopamine (DA) concentration without change in DA turnover in some forebrain DA nerve terminal systems. A selective reduction in DA turnover was observed in the medial palisade zone of the median eminence at 70 ppm $MeCl_2$. $MeCl_2$ dose-dependently increased noradrenaline (NA) turnover in the anterior periventricular hypothalamic area and dose-dependently decreased NA concentrations in the posterior preiventricular area. 1000 ppm $MeCl_2$ increased NA turnover in the anteromedial frontal cortex and reduced NA concentrations in the dorsomedial hypothalamic nucleus. No significant changes were observed in the secretion of the anterior pituitary hormones. | Fuxe et al., 1984 |
| 1000 and 5000 ppm $MeCl_2$ | Rats were exposed to $MeCl_2$ continuously for up to 14 weeks. Body and organ weights measured and gross examinations conducted. | 2 groups of 20 male Sprague-Dawley rats and 20 controls | Feed consumption was reduced. Little visible evidence of toxicity. At 5000 ppm $MeCl_2$, initial weight loss and then subnormal weight gains observed. At 1000 ppm, weight gains were subnormal after 6 weeks. No rats died during the study altough some were killed for evaluation of lesions and organ weights. No significant differences observed in treated and control rat organ weights. Lesions were "unspectacular"; mottled livers observed in 40 percent of rats that were exposed to 5000 ppm $MeCl_2$ for 14 weeks. | Haun et al., 1977;<br>MacEwen et al., 1972 |
| 500 ppm $MeCl_2$ | Rats were exposed to $MeCl_2$ 8 hr per day 5 days per week for 15 weeks. | 16 young treated rats, unspecified strain, and 16 controls | 3 exposed rats within the first 6 weeks and none of the control rats died. The rats gained weight rapidly and all the survivors appeared in "excellent" condition throughout the study. | Heppel et al., 1944 |
| 1100 ppm $MeCl_2$ | Rats were exposed to $MeCl_2$ 8 hr per day 5 days per week for 15 weeks. | 16 young rats, unspecified strain | Weight gains were observed during the study and "many" litters were born. | Heppel et al., 1944 |
| 5000 ppm (17 mg/l) $MeCl_2$ | Rats were exposed to $MeCl_2$ 7 hr per day 5 days per week for a total of 42 to 132 exposures. Animals were necropsied at the end of the experiment. | 15 treated male and 6 female rats, unspecified strain, and 28 controls | 1 rat died at 22 exposures after giving birth to a litter; many thrombi in renal vessels and marked cortical infarction were observed. Rats appeared well and no narcosis was observed during the experiment. | Heppel et al., 1944 |
| 10000 ppm (34 mg/l) $MeCl_2$ | Rats were exposed to $MeCl_2$ for 6 hr 1 day and then 4 hr daily 5 days a week for a total of 38 exposures. Histopathological studies were performed at the end of the experiment. | 9 male and 7 female rats, unspecified strain | 2 rats died after 33 and 38 exposures, respectively. The second dead rat had marked pulmonary congestion and edema with focal extravasation of blood. One surviving rat had similar but less marked pulmonary changes. Rats gained weight rapdily during exposure period. | Heppel et al., 1944 |

TABLE 6 - Continued

SUBCHRONIC AND CHRONIC INHALATION STUDIES

| Material and Concentration Tested | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 5000 ppm $MeCl_2$ | Rat running activity scores, calculated as the number of revolutions of a rotating drum, were measured for 1 hr before, during, and 30 min after exposure to $MeCl_2$. Five trials were conducted, one every other day. | 5 young male rats, unspecified strain | $MeCl_2$ did not have a depressant effect on rats but running activity scores, measured in the experiment, were significantly less during exposure. | Heppel et al., 1944 |
| 500 and 1000 ppm, 1000 ppm as a time-weighted average (TWA) (100 to 2800 ppm) $MeCl_2$ | Rats were exposed to $MeCl_2$ 6 hr daily 5 days a week for 2 weeks. The rats were killed, microsomes prepared from kidneys and livers and enzyme activities were determined. | 3 groups of 10 treated male Wistar rats and 10 controls | Hepatic microsomal UDP-glucuronosyltransferase activity increased dose- dependently after 5 and 10 days of exposure and hepatic NADPH cytochrome c-reductase activity decreased in a parallel manner. No change in hepatic cytochrome P-450 content, ethoxycoumarin O-deethylase activity, or glutathione content. Renal ethoxycoumarin deethylase activity increased dose-dependently after 5 and 10 days. Cytochrome P-450 content had a tendency to increase. Ater 10 days, renal glutathione content was increased. | Kurppa and Vainio, 1981 |
| 10000 ppm $MeCl_2$ | Rats were exposed to $MeCl_2$ 6 hr daily for 90 days. Hematologic, clinical chemistry, and urine parameters were measured. Rats were killed and histologic exams were performed. | 20 male and 20 female treated Sprague-Dawley rats and 20 male and 20 female controls | Slight redness of the conjunctivae was observed for 1 to 10 hr after each exposure. No other signs of toxicity were observed and no rats died. An incidental differing adrenal weight and occasional changes in lungs and other organs were observed but these changes were not due to $MeCl_2$. | Leuschner et al., 1984 |
| 0, 1625, 3250, 6500, 13000, and 16000 ppm $MeCl_2$ | Rats were exposed 6 hr a day, 5 days a week for 19 days (total of 11 exposures). Necropsies were performed on all rats. | Groups of 5 male and female F344/N rats. | 4 of 5 male and all of 5 female rats exposed to 16000 ppm $MeCl_2$ and 1 of 5 male and 1 of 5 female rats exposed to 13000 ppm $MeCl_2$ died during the study. Final mean body weights of surviving males exposed to 13000 and 16000 ppm $MeCl_2$ and surviving females exposed to 6500 and 13000 ppm $MeCl_2$ lower than control rats. Intermittent scratching, ataxia, and hyperactivity were observed in all except the 2 lowest dosed groups. Dyspnea and anesthesia were observed in all rats exposed to 13000 and 16000 ppm $MeCl_2$. | NTP, 1986 |
| 0, 525, 1050, 2100, 4200, and 8400 ppm $MeCl_2$ | Rats were exposed 6 hr a day, 5 days a week for 13 weeks (total of 63 exposures). Necropsies were performed on all rats. | Groups of 10 male and female F344/N rats. | 1 of 10 male and 1 of 10 female rats exposed to 8400 ppm $MeCl_2$ died during the study. Final mean body weights of male and female rats exposed to 8400 ppm $MeCl_2$ were lower than those of controls. Mild to minimal lung changes were observed; foreign body pneumonia or a focal accumulation of mononuclear and multinucleated inflammatory cells were present in 4 of 10 male and 6 of 10 female rats exposed to 8400 ppm $MeCl_2$ and in 1 of 10 female rats exposed to 4200 ppm $MeCl_2$. The liver lipid:liver weight ratios for male and female rats exposed to 8400 ppm $MeCl_2$ were significantly lower than those of controls. | NTP, 1986 |

TABLE 6 - Continued

SUBCHRONIC AND CHRONIC INHALATION STUDIES

| Material and Concentration Tested | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 250, 500, and 5000 ppm $MeCl_2$ | Rats were exposed 5 hr daily for 10 days to 500 and 5000 ppm $MeCl_2$ or for 28 days to 250 ppm $MeCl_2$. Rats were killed, liver microsomal preparations were prepared and enzyme activities determined. Histological studies were made of the liver. | Groups of 5 to 6 treated male SPF-Wistar rats and 15 to 50 controls | 10 days of 5000 ppm $MeCl_2$ produced a significant increase in hepatic cytochrome P-450 content. 10 days of 5000 ppm $MeCl_2$ produced a significant increase in microsomal aminopyrine demethylase activity. 28 days of 250 ppm $MeCl_2$ caused no significant changes in these parameters. No abnormal changes in livers were observed. | Norpoth et al., 1974 |
| 4000 ppm $MeCl_2$ | Rats were exposed to $MeCl_2$ 4 hr daily 5 days per week for 4 weeks. Pulmonary secretions were obtained by lavage and glycosaminoglycans were characterized. | 10 Osborne-Mendel rats and unspecified number of control rats | Glycosaminoglycans were isolated from the pulmonary secretions of treated but not control rats. Hyaluronic acid was the only glycosaminoglycan present in detectable amounts. The researchers stated that this glycosaminoglycan may be an indication of pulmonary injury. | Sahu and Ulsamer, 1980 |
| 3700 ppm $MeCl_2$ | Rats were exposed to $MeCl_2$ 5 hr daily 5 days per week for 4 weeks. Pulmonary secretions were obtained by lavage and various enzymes, protein, hexose, and sialic acid contents were determined. | Unspecified number of male and female treated Sprague-Dawley rats and control rats | There was an increase in protein, hexose, sialic acid, acid phosphatase, alkaline phosphatase, and acetate dehydrogenase in the treated rat pulmonary lavage. The researchers stated that these parameters were useful as indicators of pulmonary injury induced by inhalation of $MeCl_2$. | Sahu et al., 1980 |
| 4000 ppm $MeCl_2$ | Rats were exposed to $MeCl_2$ 5 hr daily 5 days per week for 4 weeks. Rats were killed, pulmonary secretions were obtained by lung lavage and then the lungs were removed and homogenated. Lipid peroxidation was estimated. | Male and female Sprague-Dawley rats and control rats | $MeCl_2$ inhalation resulted in increased lipid peroxidation in both lung secretions and pulmonary tissues. | Sahu and Lowther, 1981 |
| 500 and 1000 ppm, 1000 ppm as a TWA (100 to 2800 ppm) $MeCl_2$ | Rats were exposed to $MeCl_2$ 6 hr daily 5 days a week for up to 2 weeks. 5 rats were killed after 5 exposures and 5 after 10 exposures. 5 rats were observed for 7 days after exposure. Brain was sampled and and enzyme activities determined. | 3 groups of 15 treated male Wistar rats and 15 controls | With 1000 ppm $MeCl_2$, cerebral acid proteinase activity was decreased at 1 week and increased at 2 weeks and cerebellar succinate dehydrogenase activity was decreased at 1 week. With 1000 ppm $MeCl_2$ as a TWA, cerebral RNA content was increased at 2 weeks, cerebral NADPH-diaphorase activity decreased at 1 week and increased at 2 weeks, cerebellar succinate dehydrogenase was increased at 2 weeks, and cereberall succinate dehydrogenase activity was decreased at 1 and at 2 weeks. 7 days after exposure, with 1000 ppm $MeCl_2$, cerebral RNA content was decreased, and with 1000 ppm $MeCl_2$ as a TWA, both cerebral and cerebellar succinate dehydrogenase activities were decreased. The researchers suggested that several days of recovery were necessary to restore the oxidative capacity of the brain cells. Additionally, exposure to 1000 ppm as a TWA produced a larger burden and greater neurochemical effects than exposure to a stable concentration of $MeCl_2$. | Savolainen et al., 1981 |

TABLE 6 - Continued

SUBCHRONIC AND CHRONIC INHALATION STUDIES

| Material and Concentration Tested | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 500 ppm $MeCl_2$ | Rats were exposed to $MeCl_2$ 6 hr daily for 4 days. Animal behavior was studied in an open-field situation 1 and 17 hr after the last exposure. Two rats were killed 17 hr later and two rats were further exposed for 2 hr, 2 for 3 hr, 2 for 4 hr and 2 for 6 hr on the fifth day. The rats were killed and brain and liver removed and enzyme activities determined. | 10 treated male Wistar rats and 10 controls | Preening frequency and time was significantly increased 1 hr after the last exposure. Brain acid proteinase activity was highest in rats exposed to $MeCl_2$ for 3 and 4 hr on the fifth day. The highest content of hepatic microsomal cytochrome P-450 was found in rats exposed to $MeCl_2$ for 2 hr on the fifth day; it decreased at 3 and 4 hr on the fifth day. | Savolainen et al., 1977 |
| 500, 1500, and 3000 ppm $MeCl_2$ | Rats were exposed to $MeCl_2$ 6 hr daily for 3 days and were killed on the fourth day. Rat liver microsomes were prepared and enzyme assays were performed. | Groups of 4 treated male Sprague-Dawley rats and 4 controls | There were no signs of general toxicity. 500 ppm $MeCl_2$ caused a small but significant reduction in hepatic microsomal cytochrome P-450 concentration. No changes were observed with 1500 and 3000 ppm $MeCl_2$. The metabolic activity of cytochrome P-450 was altered. | Toftgard et al., 1982 |
| 2000 and 4000 ppm | Rats were exposed to $MeCl_2$ 6 hr/day for 10 days and were killed on day 11. Lungs and livers were examined. | Groups of 10 male Fischer 344 rats and 10 controls. | $MeCl_2$ had a mild anaesthetic effect. Body weight gains were reduced in the 4000 ppm group and initially increased in the 2000 ppm group. Increased eosinophilia of the hepatic centrolobular cells observed; an increased incidence of mitotic figures in the midzonal region adjacent to the zone of increased eosinophilia in the 4000 ppm group was noted. No pulmonary changes observed. Lipid and glycogen accumulated in the centrolobular cells of rat liver. | ICI, 1986a |
| 1000 and 5000 ppm $MeCl_2$ | Mice were exposed to $MeCl_2$ continuously for up to 14 weeks. | 2 groups of 380 female ICR mice and 380 controls | Narcotic effects in mice at 5000 ppm during the first day; mice remained lethargic throughout the experiment. Feed consumption was reduced. At 5000 ppm $MeCl_2$, 23 mice were dead by 4 days and 100 more were dead by one month; the other mice at this exposure concentration were killed then. 10 mice exposed to 1000 ppm $MeCl_2$ died by the end of 14 weeks. | Haun et al., 1971; MacEwen et al., 1972 |
| 0, 1625, 3250, 6500, 13000, and 16000 ppm $MeCl_2$ | Mice were exposed 6 hr a day, 5 days a week for 19 weeks (total of 11 exposures). Necropsies were performed on all mice. | Groups of 5 male and 5 female $B6C3F_1$ mice. | All the mice exposed to 16000 ppm $MeCl_2$ and 3 of 5 male mice and 4 of 5 female mice exposed to 13000 ppm $MeCl_2$ died during the study. The surviving female mouse exposed to 13000 ppm $MeCl_2$ lost weight. The final body weights of all other groups of dosed and control mice were comparable. Compound-related hyperactivity was observed. No $MeCl_2$-related effects were observed at necropsy. | NTP, 1986 |
| 0, 525, 1050, 2100, 4200, and 8400 ppm $MeCl_2$ | Mice were exposed 6 hr a day, 5 days a week for 13 weeks (total of 63 exposures). Necropsies were performed on all mice. | Groups of 10 male and and 10 female $B6C3F_1$ mice. | 4 of 10 male and 2 of 10 female mice exposed to 8400 ppm $MeCl_2$ died during the study. Final mean body weights of female mice exposed to 8400 ppm $MeCl_2$ were less than those of controls. Hydropic changes were observed in liver, and liver lipid:liver weight ratios for female mice exposed to 8400 ppm $MeCl_2$ were significantly lower than those of controls. | NTP, 1986 |

TABLE 6 - Continued

SUBCHRONIC AND CHRONIC INHALATION STUDIES

| Material and Concentration Tested | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 1000 and 5000 ppm $MeCl_2$ | Mice were continuously exposed to $MeCl_2$ for 4 weeks and spontaneous activity was determined. | Groups of 10 female white mice | By day 7, 50 percent of the mice exposed to 5000 ppm $MeCl_2$ died and, therefore, determinations of spontaneous activity were discontinued. The mice exposed to 1000 ppm $MeCl_2$ survived for 4 weeks. When compared to the pre-exposure baseline period, there was a definite trend toward lower activity during exposure. Activity stabilized at a lower level during the second 2 week exposure period than during the first 2 week exposure period. | Thomas et al., 1971 |
| 5000 ppm $MeCl_2$ | Mice were continuously exposed to $MeCl_2$ for up to 7 days. Groups of mice were killed after 1, 4, 8, and 12 hr and 1, 2, 3, 4, 6, and 7 days. Livers and other organs were removed, weighed, and examined by light and electron microscopy and hepatic triglycerides were measured. Amino acid incorporation was determined by intravenous injections of radioactive leucine. | Groups of 4 to 20 treated female ICR mice and controls | During the first few hours, increased spontaneous activity and decreased feed and water intake was observed. At 24 hr, the mice were lethargic and dehydrated and had a "hunched" posture and roughened hair coat. During the next 48 hr, these signs persisted and the hair was yellowed and had a greasy appearance. At 96 hr, some of these changes were reversed. At 1 week, treated mice were almost as active as the controls but were emaciated and dehydrated and still had a roughened coat. Treated mice lost weight during exposure. Hepatic triglycerides increased to a peak at 3 days and then decreased until 6 days when they plateaued at a concentration greater than in the controls. Exposure to $MeCl_2$ caused ballon degeneration and transient severe fatty change in the liver and partial inhibition of leucine incorporation into hepatic proteins. The earliest lesion was observed at 12 hr of exposure. Some changes were partially reversed during exposure. The researchers stated that the reversibility of hepatic changes suggested that partial hepatocyte tolerance was developed following continuous exposure to $MeCl_2$. | Weinstein et al., 1971; 1972 |
| 5000 ppm $MeCl_2$ | Mice were exposed 6 hr daily for 4 days. The mice were killed and the livers were examined by light and electron microscopy. | Treated female ICR mice and controls | There was an increase in lipid content and a decrease in glycogen content of hepatocytes. Polysomes were intact and cisternae of rough endoplasmic reticulum were of normal configuration. Early changes are reversible during the 18 hr non-exposure period between the exposure periods. | Weinstein et al., 1971 |
| 2000 and 4000 ppm | Mice were exposed to $MeCl_2$ 6 hr/day for 10 days and were killed on day 11. Lungs and livers were examined. | Groups of 10 male B6C3F1 mice and 10 controls. | $MeCl_2$ had a mild anaesthetic effect. Dose-related statistically significant increases in body weight and increases in liver weights and liver/body weight ratios observed. No hepatic changes. No pulmonary changes of significance were observed. Pale, enlarged mitochondria were observed in pulmonary cells. There was an increase in myelin whorls in the bile canaliculi of the centrolobular hepatocytes and an accumulation of glycogen in the 4000 ppm group. | ICI, 1986a |

TABLE 6 - Continued

SUBCHRONIC AND CHRONIC INHALATION STUDIES

| Material and Concentration Tested | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 210, 350 and 700 ppm $MeCl_2$ | Gerbils exposed by continuous inhalation for up to 3 months, then treatment-free for 4 months. Brains homogenized and proteins and DNA measured. | Groups of 10 male and 10 female gerbils. 40 sex-matched lifetime controls | High mortality was observed at 2 higher doses and exposure terminated at 10 and 7 weeks, respectively. Increased brain concentrations of 2 astroglial proteins and decreased cerebellar DNA observed with 2 higher $MeCl_2$ doses. | Rosengren et al., 1986 |
| 552 to 11100 ppm $MeCl_2$ | Animals were exposed to 560, 5000, or 11100 ppm $MeCl_2$ for 6 hr or to 552 to 679 ppm $MeCl_2$ for 6 hr daily for 5 days. These animals were anesthetized with sodium pentobarbital, blood was sampled, lung, liver, kidney, and spleen were examined and sectioned, and the liver was homogenated for triglyceride measurement. | Groups of 3 to 10 male Hartley guinea pigs | At the beginning of the 6 hr 11100 ppm exposure, the guinea pigs exhibited continuous motion of both fore and hind limbs while lying on their side or back. 4 of 10 animals died at the 6 hr 11100 ppm exposure. Weight loss was observed with 5 day $MeCl_2$ exposure. Hepatic triglycerides were significantly increased with 6 hr 5000 and 11100 ppm and 5 day $MeCl_2$ exposures. Arterial carboxyhemoglobin was increased at all 6 hr exposures. All kidneys and spleens were normal in appearance. The lung of 1 of 5 animals at 6 hr 11100 ppm $MeCl_2$ was hemmorhagic; 3 of these 5 had microscopic evidence of congestion and hemorrhage. 5 days of $MeCl_2$ produced more pneumonitis than was evident in the controls. 6 hr of 5000 or 11000 ppm and 5 days of $MeCl_2$ resulted in mottled livers. 6 hr of 11100 ppm and 5 days of $MeCl_2$ resulted in minimal fatty change, moderate mid-zonal fatty change, and diffuse fat vacuolization in the liver. Minimal to moderate hepatic changes were found at the other exposure regimens. | Balmer et al., 1976 |
| 500 ppm $MeCl_2$ | Guinea pigs were exposed to $MeCl_2$ 8 hr per day 5 days per week for 15 weeks. | 16 young treated guinea pigs and 16 controls | One of the exposed guinea pigs died and two of the of the controls died. The guinea pigs gained weight rapidly and all the survivors appeared in "excellent" condition throughout the study. | Heppel et al., 1944 |

TABLE 6 - Continued

SUBCHRONIC AND CHRONIC INHALATION STUDIES

| Material and Concentration Tested | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 1100 ppm $MeCl_2$ | Guinea pigs were exposed to $MeCl_2$ 8 hr per day 5 days per week for 15 weeks. | 16 young treated guinea pigs and 16 controls | One exposed and two control guinea pigs died. The guinea pigs did gain weight during the study. | Heppel et al., 1944 |
| 5000 ppm (17 mg/l) $MeCl_2$ | Guinea pigs were exposed to $MeCl_2$ 7 hr per day 5 days per week for a total of 65 to 131 exposures. Animals were necropsied at the end of the experiment. | 14 treated guinea pigs and 14 controls | 3 treated guinea pigs died after 35, 90, and 96 exposures, respectively, and none of the controls died; extensive pneumonia and moderate fatty centro-lobular fatty degeneration of the liver was observed. The guinea pigs appeared "well nourished" and survivors did thrive, but the treated animals did not eat as much and did not gain as much weight as the controls. | Heppel et al., 1944 |
| 10000 ppm (34 mg/l) $MeCl_2$ | Guinea pigs were exposed to $MeCl_2$ for 6 hr 1 day and then 4 hr daily 5 days a week for a total of 38 exposures. Histopathologic studies were performed at the end of the experiment. | 11 male and 1 female treated guinea pigs and 4 controls | No guinea pigs died. Their weight gain was less than that of the control animals. Increasing somnolence was observed with exposure. No mucous membrane irritation was observed. Mild incoordination was observed. Recovery occurred within 1 hr after exposure. 4 of 6 treated guinea pigs and one control had moderate fatty degeneration of the liver. | Heppel et al., 1944 |
| 500 ppm $MeCl_2$ | Rabbits were exposed to $MeCl_2$ 8 hr per day 5 days per week for 15 weeks. Blood was sampled weekly and clinical chemistry parameters were determined. | 4 rabbits | No rabbits died. No significant changes were observed in red cell, white cell, and differential counts and hemoglobin determinations. There was a slight increase in eosinophils after the eighth week of exposure. | Heppel et al., 1944 |
| 1100 ppm $MeCl_2$ | Rabbits were exposed to $MeCl_2$ 8 hr per day 5 days per week for 15 weeks. Blood tests were performed. | 4 rabbits | Two female rabbits died after giving birth to litters. Blood test results were normal except that both female rabbits had leucopenia shortly before death. | Heppel et al., 1944 |
| 5000 ppm (17 mg/l) $MeCl_2$ | Rabbits were exposed to $MeCl_2$ 7 hr per day 5 days per week for a total of 124 to 131 exposures. Hematological parameters were measured during the experiment. Histopathologic studies were performed at the end of the experiment. | 2 male and 2 female rabbits | No rabbits died and all appeared "well nourished." No narcosis was observed. Both females bore litters but did not raise them. No hematological abnormalities were observed. No lesions were observed. | Heppel et al., 1944 |
| 10000 ppm (34 mg/l) $MeCl_2$ | Rabbits were exposed to $MeCl_2$ for 6 hr 1 day and then for 4 hr daily 5 days a week for a total of 37 exposures. Histopathologic studies were performed at the end of the experiment. | 5 male rabbits | 3 rabbits died after 1, 12, and 22 exposures, respectively. Rabbits were at first excited and then inactive. Two of these rabbits had pulmonary congeston and edema with focal necrosis, and splenic congestion. | Heppel et al., 1944 |
| 1100 ppm $MeCl_2$ | Cats were exposed to $MeCl_2$ 8 hr per day 5 days per week for 15 weeks. | 4 cats | The cats "did not seem to thrive." No signs were observed except for sleepiness and reduced activity in the beginning of the study. | Heppel et al., 1944 |

TABLE 6 - Continued

SUBCHRONIC AND CHRONIC INHALATION STUDIES

| Material and Concentration Tested | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 1000 and 5000 ppm $MeCl_2$ | Dogs were exposed to $MeCl_2$ continuously for up to 8 weeks. Body and organ weights measured, gross examinations conducted, clinical chemistry tests performed, and serum activities and liver function measured. | 2 groups of 8 female treated dogs and 8 controls | Noticeable narcotic effects at 5000 ppm during first day; coordination regained by second day but dogs remained lethargic. Food consumption reduced and progressively extreme emaciation observed. At 5000 ppm $MeCl_2$ 4 of 8 dogs were dead at one month; the other 4 dogs were killed then. At 1000 ppm $MeCl_2$, 6 of 8 dogs were dead at 2 months; the other 2 dogs were killed then. Elevated hematocrit, hemoglobin and red blood cell values at 4 weeks of 1000 ppm $MeCl_2$. SGPT and isocitric dehydrogenase (ICDH) elevated and BSP retention was increased in dogs exposed to 1000 ppm $MeCl_2$. The researchers stated there was evidence of deleterious hepatic changes in exposed dogs. Grossly yellow, fatty livers and jaundice were observed in all cases. Edema of the brain was observed in 3 dogs exposed to 5000 ppm $MeCl_2$. | Haun et al., 1971;<br>MacEwen et al., 1972 |
| 500 ppm $MeCl_2$ | Dogs were exposed to $MeCl_2$ 8 hr per day 5 days per week for 15 weeks. | 2 dogs | No dogs died. | Heppel et al., 1944 |
| 500 ppm $MeCl_2$ | Pups were born in the exposure chamber and were exposed to $MeCl_2$ 8 hr per day 5 days per week for 15 days. | 2 pups | No pups died. | Heppel et al., 1944 |
| 5000 ppm (17 mg/l) $MeCl_2$ | Dogs were exposed to $MeCl_2$ 7 hr per day 5 days per week for a total of 132 exposures. Blood pressures were measured, clinical chemistry tests and urinalysis were performed, BSP retention was determined, and hematological parameters were measured during the experiment. Histopathologic studies were performed at the end of the experiment. | 1 male and 5 female treated dogs and unspecified number of controls. | No dogs died and no ill effects were observed. Dogs appeared "well nourished" and appetites were usually excellent. No abnormal results were observed in the parameters measured except for an "insignificant tendency" for the red cell count "to rise" in 3 exposed dogs. No abnormal histopathological findings. | Heppel et al., 1944 |
| 5000 ppm (17 mg/l) $MeCl_2$ | Pups were born in the exposure chamber and exposed to $MeCl_2$ 7 hr per day 5 days per week for a total of 115 exposures. | 1 male and 1 female pup. | No pups died and they gained weight. | Heppel et al., 1944 |
| 10000 ppm (34 mg/l) $MeCl_2$ | Dogs were exposed to $MeCl_2$ for 6 hr for 1 day and then for 4 hr daily 5 days a week for a total of 6 exposures. Histopathological examination of the livers was performed. | 4 female dogs | No dogs died. However, they engaged in wild, aimless movements during exposure; they frothed at the mouth, and conjunctival irritation developed. After exposure, they recovered rapidly. Moderate centrolobular congestion with narrowing of hepatic cell cords and slight to moderate fatty degeneration of the liver was observed in 2 dogs. | Heppel et al., 1944 |

**TABLE 6 - Continued**

**SUBCHRONIC AND CHRONIC INHALATION STUDIES**

| Material and Concentration Tested | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 5000 ppm $MeCl_2$ | Dogs were exposed to $MeCl_2$ 6 hr daily for 90 days. Hematologic, clinical chemistry, and urine parameters were measured. Electrocardiograms were made and circulatory functions were examined. Dogs were killed and histologic examinations were performed. | 3 male and 3 female treated Beagle dogs and 3 male and 3 female controls | Slight sedation was induced throughout the exposure period. All dogs had slight erythema, lasting up to 10 hr after exposure. No other signs of toxicity were observed and no dogs died. Isolated changes in various organs were not due to $MeCl_2$. | Leuschner et al., 1984 |
| 500 ppm $MeCl_2$ | Monkeys were exposed to $MeCl_2$ 8 hr per day 5 days per week for 15 weeks. | 2 rhesus monkeys | No monkeys died. | Heppel et al., 1944 |
| 10000 ppm (34 mg/l) $MeCl_2$ | Monkeys were exposed to $MeCl_2$ for 6 hr for 1 day and then for 4 hr daily 5 days a week for a total of 36 to 37 exposures. Histopathologic studies were performed at the end of the experiment. | 2 female monkeys | The monkeys lay prostate during the first exposures but in the last 2 weeks sat up throughout. They gained weight. No abnormal histopathologic findings were observed except that one monkey had disseminated tuberculosis lesions. | Heppel et al., 1944 |
| 1000 and 5000 ppm $MeCl_2$ | Monkeys were exposed to $MeCl_2$ continuously for up to 4 weeks. Body and organ weights were measured, gross examinations conducted, clinical chemistry tests performed, and serum enzyme activities and hepatic function measured. | 2 groups of 4 rhesus monkeys and 4 controls | Narcotic effects in monkeys at 5000 ppm $MeCl_2$ during first day; coordination regained by second day but monkeys remained lethargic. Food consumption reduced and progressive emaciation observed. At 5000 ppm, severe weight losses were observed. One monkey exposed to 5000 ppm died at 2 weeks and the other 3 monkeys were killed then. At 1000 ppm, monkeys survived for 14 weeks. They lost weight at 2 weeks, regained it at 4 weeks, and maintained their weights for the rest of the study. At 1000 ppm $MeCl_2$, monkeys had increased hematocrit, hemoglobin, and red blood cell values. No differences from controls in SGPT or in most ICDH activity values. BSP retention was increased. No other abnormal clinical chemistry values observed. The researchers stated that there was evidence of deleterious hepatic changes in exposed monkeys. Borderline hepatic changes in 3 monkeys exposed to 5000 ppm $MeCl_2$. No gross lesions seen in monkeys exposed to 1000 ppm. | Haun et al., 1971; MacEwen et al., 1972 |
| 0.5 and 5.0 mg/l of a deodorant containing 21.5 percent $MeCl_2$ | One group of monkeys exposed to 1 sec spray of deodorant at 42 min intervals 6 hr daily (0.5 mg/l) 5 days per week for 90 days and one group exposed to 5 sec spray at 21 min intervals 6 hr daily (5.0 mg/l) 5 days per week for 90 days. At 90 days, opthalmoscopic examination performed. Prior to exposure and at 30 and 90 days, electrocardiograms were made and tidal volume and respiratory rate, and clinical blood and urine parameters were measured. At 90 days the monkeys were killed and histopathological and microscopic examinations were performed. | Groups of 3 male and 3 female treated and control stumptail monkeys | All monkeys survived the experiment and no significant behavioral or body weight changes were observed. All clinical blood and urine parameters were normal. Electrocardiograms and tidal and respiratory volumes were normal. No ocular abnormalities were observed in the 0.5 mg/l group. All animals in the 5.0 mg/l group had an observeable lens nuclear outline. Gross and microscopic pathological examination of tissues were negative for formulation-induced changes. | Meltzer et al., 1977 |

## TABLE 7

## ACUTE INTRAPERITONEAL STUDIES

| Material Tested | Method | No. and Species of Animal | LD50 | Results and Comments | References |
|---|---|---|---|---|---|
| $MeCl_2$ in peanut oil | 0, 0.2, 0.5, and 1.0 ml/kg $MeCl_2$ administered intraperitoneally to rats. Rats killed at an unspecified time after dosing, serum glutamic oxaloacetic transaminase (SGOT) activity determined as a measure of hepatoxicity, and liver sampled for histopathologic studies. | Male Sprague-Dawley rats (unspecified but probably groups of 5) | - - - | 3 of 5 rats died at the 1.0 ml/kg dose. At all doses, SGOT activity was greater than in the controls. Livers of treated rats were not "markedly" different from livers of control rats. | Cornish et al., 1973 |
| 1 ml $MeCl_2$ in 10 ml olive oil | Rats fasted for 18 hr were administered 0.2 ml olive oil solution intraperitoneally and killed 40 hr later. Blood was sampled for enzyme activity determinations as a measure of hepatic injury and livers were sampled for histological analyses. | Male Wistar rats (unspecified but probably groups of 5) | - - - | Serum glutamic-pyruvic transaminase (SGPT) activity increased significantly and SGOT activity increased but not significantly when compared to controls. Ornithine carbamyl-transferase (OCT) activity also increased significantly. There was no difference observed in the liver of the treated and control rats. | Corsi et al., 1983 |
| 50 percent $MeCl_2$ solution in corn oil | 0.65 ml/kg $MeCl_2$ administered intraperitoneally to rats and control rats received 2 ml/kg corn oil. Rats fasted for 24 hr and then anesthetized and common bile duct cannulated at 2 sites to measure hepatic bile flow and bile duct-pancreatic fluid (BDPF) flow over a 4 hr period. Pancreas removed and examined. | Groups of 4 to 6 male Sprague-Dawley rats | - - - | $MeCl_2$ caused an increase in BDPF flow. BDPF chloride, potassium, and sodium concentrations increased significantly and protein concentration decreased. There was no significant change in the bicarbonate concentration, pancreatic weight, or hepatic bile flow. In a similar experiment with a marker compound injected into the biliary tree of rats, an increase in BDPF was also observed (Harms et al., 1976). | Hamada and Peterson, 1977 |
| $MeCl_2$ in corn oil | 1330 mg/kg $MeCl_2$ (total volume of 4 ml/kg) administered intraperitoneally to rats. Rats killed 2, 12, 24, 48, and 96 hr later and kidneys removed for histopathological and functional studies. Organic ion accumulation by renal slices was determined. | Groups of 6 male Fischer 344 rats | - - - | Potassium concentration in renal intracellular water not different from controls at 24 hr. Fraction of water in renal tissue was increased with the greatest increase at 24 hr. Kidneys weight was increased. $MeCl_2$ caused some proximal tubular swelling in the cortex and outer medulla but had no effect on glomerular, distal tubular, inner medullary or papillary cell morphology. Renal reduced nonprotein sulfhydryls concentration (largely reduced glutathione) were at a minimum concentration 2 hr after treatment and were not different from the controls but at 24 hr were at a maximum concentration and were increased by $MeCl_2$. | Kluwe et al., 1982 |

TABLE 7 - Continued

ACUTE INTRAPERITONEAL STUDIES

| Material Tested | Method | No. and Species of Animal | LD50 | Results and Comments | References |
|---|---|---|---|---|---|
| $MeCl_2$ | 1 to 6 mmol/kg $MeCl_2$ administered intraperitoneally to rats. Rats anesthethized with hexobarbital and sciatic motor conduction velocity determined 2 hr later. | Male albino rats | - - - | There was a positive linear correlation between dose of $MeCl_2$ and sciatic motor conduction velocity. The researchers stated that this may be due to endogenous carbon monoxide production from $MeCl_2$ metabolism. | Pankow et al., 1979 |
| $MeCl_2$ in mineral oil | Rats fasted overnight, 90 µl/100 g $MeCl_2$ administered intraperitoneally, breath samples collected from 3 rats 15, 30, 60, 90, and 120 min later and pentane production, a measure of lipid peroxidation, was determined. Rats given up to 270 µl/100 g $MeCl_2$ killed 30 min later and conjugated dienes, which represent lipid hydroperoxides, measured in various organ homogenates. | Male Sprague-Dawley rats | - - - | Pentane production in treated rats not different from control rats given only mineral oil. $MeCl_2$ did not induce diene conjugation in liver, lungs, kidneys, intestine, spleen, and heart. The researchers stated that $MeCl_2$ did not induce lipid peroxidation. | Sagal and Tappel, 1979 |
| $MeCl_2$ | $MeCl_2$ administered intraperitoneally to mice, mice killed at 0.5 and 1 hr, brain striatum removed and homogenized. Four experiments performed. | Groups of 3 male albino Swiss mice | - - - | At 0.5 hr following $MeCl_2$ administration, mouse striatal p-tyramine was significantly increased and at 1 hr, striatal m-tyramine was significantly increased. | Juorio and Yu, 1985 |
| $MeCl_2$ in corn oil | $MeCl_2$, in a 0.01 ml/kg volume, administered intraperitoneally to mice, number of deaths at 24 hr recorded for LD50 and mice observed a further 10 days. Hepatic function assessed in treated mice by injecting sulfobromophthalein (BSP) intravenously and sampling blood and determining BSP retention 30 min later and by measuring SGPT activity. Renal function was assessed by injecting phenolsulfonephthalein (PSP) intravenously and collecting the urine and measuring PSP, protein, and glucose excretion. Mice treated and killed for histopathologic studies of liver and kidneys. | 4 to 5 groups of male Swiss-Webster mice for LD50 study. Unspecified number treated and 59 to 77 controls for liver and kidney function studies. Two groups of 4 to 6 mice treated for histopathologic studies. | 1.5 ml/kg (23 mmol/kg) | In LD50 study, no further deaths observed after 24 hr. 24 hr after $MeCl_2$ treatment (dose unspecified), there was no increase in BSP retention or SGPT activity. Histopathologically, the livers of treated mice were essentially the same as the controls with only a mild inflammatory change seen with high lethal doses. There was no delay in renal PSP excretion and no increase in urinary glucose or protein. When $MeCl_2$ was administered in the lethal range, a few kidneys had hydropic degeneration with a minimal amount of necrosis of the convoluted tubules. The researchers stated that they observed no hepatic or renal dysfunction following $MeCl_2$ administration. | Klaassen and Plaa, 1966 |

TABLE 7 - Continued

ACUTE INTRAPERITONEAL STUDIES

| Material Tested | Method | No. and Species of Animal | LD50 | Results and Comments | References |
|---|---|---|---|---|---|
| $MeCl_2$ in corn oil | A 0.1 ml/10 g volume of $MeCl_2$ in corn oil was administered to mice. Doses were 1 and 1.5 ml/kg of $MeCl_2$. 24 hr later, glucose and protein were measured in the urine. Kidneys from 5 of the 1 ml/mg $MeCl_2$ treated mice were examined histologically. | Groups of 10 male Swiss mice | - - - | No significant protein or glucose concentration was observed in the urine. The 1 ml/mg dose of $MeCl_2$ did not cause swelling or necrosis of the kidneys. The researchers stated that they observed no renal dysfunction following $MeCl_2$ administration. | Plaa and Larson, 1965 |
| $MeCl_2$ in corn oil or undiluted | 100 to 1000 mg/kg $MeCl_2$ administered intraperitoneally to guinea pigs, guinea pigs anesthetized and blood sampled 24 hr later for serum OCT, a measure of hepatic damage. Guinea pigs then killed and livers removed for histopathologic studies. | Groups of 4 male guinea pigs. 117 control guinea pigs | - - - | There was no increase in comparison with the control animals in serum OCT. There was equivocal hepatic damage only at the 1000 mg/kg dose. There was no accumulation of lipid in liver cells. The researchers stated that $MeCl_2$ was not a hepatotoxin. | DiVincenzo and Krasavage, 1974 |
| $MeCl_2$ in corn oil | 0.50 to 1.25 ml/kg $MeCl_2$ was administered intraperitoneally to dogs. The LD50 was determined 24 hr later. Liver function was determined by measuring SGPT activity. Dogs were anesthetized with phenobarbital sodium, the ureters were cannulated, PSP was administered intravenously, urine was collected and PSP excretion was measured. Livers and kidneys were removed for histopathological examination from 3 to 4 survivors of the LD50 study from dogs used in the hepatic function study 48 hours after the study, and from dogs used in the renal study 24 hr after the study. | 5 mongrel male and female dogs used in LD50 study. Groups of 3 to 5 dogs used in SGPT study. Number unspecified for other studies. | 0.95 ml/kg (15 mmol/kg) | 3 dogs given 0.75 m/kg had increased SGPT activity. Normal SGPT activity was observed 24 hr after giving 2 dogs 0.5 ml/kg. At near-lethal doses, $MeCl_2$ produced neutrophilic infiltrations in the sinusoids and portal areas of the liver, but no necrosis. Near the dose of $MeCl_2$ causing elevated SGPT activity, vacuolization of centrolobular hepatocytes was observed in about half the dogs. SGPT activity was increased in 3 dogs given approximately 0.71 ml/kg $MeCl_2$ but it returned to normal in about 7 days. Renal PSP excretion in treated rats was not different from the controls. There was slight calcification of renal tubules at near-lethal doses of $MeCl_2$. | Klaassen and Plaa, 1967 |

## SUBCUTANEOUS STUDIES

Single subcutaneous doses of $MeCl_2$ have been administered to mice (Kutob and Plaa, 1962) and rabbits (Barsoum and Saad, 1934) (Table 10). The LD50 for $MeCl_2$ administered subcutaneously to male mice was 76 mmol/kg and the minimum lethal dose for death within 24 hours for rabbits was 2.7 g/kg. Subchronic subcutaneous studies with $MeCl_2$ have also been conducted with rats (Douglas et al., 1980a; Loyke, 1973) (Table 8).

## INTRAVENOUS STUDIES

Five dogs were anesthetized with ether and were given 100 to 200 mg/kg $MeCl_2$ diluted in olive oil through a cannula in the femoral vein (Barsoum and Saad, 1934). The total dose of $MeCl_2$ ranged from 0.45 to 1.34 g. The dogs were observed until death or recovery. Two of the dogs died. The minimum intravenous lethal dose in 30 minutes was 200 mg/kg.

The effect of $MeCl_2$ on the vestibular function of rats was studied by inducing nystagmus by accelerated rotation (Tham et al., 1984). Electronystagmography was performed on 15 female Sprague-Dawley rats and the veins and arteries of the tails were cannulated. A 0.1 to 10% $MeCl_2$ solution was administered by continuous 60 minute intravenous infusion at a rate of 32 µl/min. The $MeCl_2$ was dissolved in Intralipid $^{R}$, an emulsion of lipids used for human parenteral nutrition. Blood samples were analyzed for $MeCl_2$. Rotary tests were performed before infusion and afterwards at 5 min intervals, and the duration of nystagmus was measured. $MeCl_2$ had a depressive effect on the vestibulo-ocular reflex. The lower threshold limit value of the arterial blood at which depression occurred was 0.7 mM/l (60 ppm); the infusion rate was 60 mM/kg/min. This threshold value was below the threshold for signs of general toxicity; consciousness, respiration, and circulation appeared to be unaffected.

TABLE 8

ACUTE AND SUBCHRONIC SUBCUTANEOUS STUDIES

| Material Tested | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| $MeCl_2$ in olive oil | For the LD50 study, 0.5 ml/10 g volumes of $MeCl_2$ in olive oil were administered subcutaneously to mice and the mice were observed for 10 days. 19.7 and 59.0 mmol/kg $MeCl_2$ were given and 24 hr later, 45 mg/kg phenobarbital was administered intraperitoneally and the increase in sleeping time was determined. Other mice were given BSP intravenously, anesthetized with ether, and cardiac punctures were performed 15 min later for blood samples. BSP retention was measured. Histopathologic studies were performed on the livers of treated mice. | Male Swiss albino mice | The LD50 for $MeCl_2$ was 76 mmol/kg. The mean effective $MeCl_2$ dose for causing an increase in phenobarbital-induced sleeping time was 39 mmol/kq. BSP retention was not significantly increased. No lesions were observed in the livers of treated mice. | Kutob and Plaa, 1962 |
| $MeCl_2$ in olive oil | 1.0 to 3.0 g/kg (0.960 to 2.73 g total dose) $MeCl_2$ was administered subcutaneously to rabbits and the rabbits were observed for 7 days. | 6 rabbits | Two rabbits died within 24 hr. The other 4 rabbits survived. The minimum lethal dose for death within 24 hr was 2.7 g/kg. | Barsoum and Saad, 1934 |
| $MeCl_2$ | 0.15 ml/100 g $MeCl_2$ administered subcutaneously to one group of normotensive control (NC) rats and spontaneously hypertensive (SH) rats daily for 5 days and to one group weekly for 5 weeks. Blood pressure and body weights were measured daily or weekly. Blood was sampled 72 hr after the last $MeCl_2$ dose and plasma renin activity determined in the rats that received $MeCl_2$ daily for 5 days. The rats were killed after the last $MeCl_2$ dose and tissues removed and compared with tissues from untreated rats. | 12 NC and 12 SH Wistar Kyoto rats in 1 wk study. 12 of each in 5 wk study. Unspecified number of controls for for these studies. 4 NC and 4 SH untreated control rats for tissue comparison. | There were no significant differences in the body weights of NC or SH treated rats and untreated rats. No difference in blood pressure was observed in NC rats treated for 5 days or untreated but the blood pressure of the SH rats treated for 5 days was reduced by $MeCl_2$. Plasma renin activity was unchanged by $MeCl_2$. Blood pressure was not reduced in the NC and SH rats treated for 5 weeks. $MeCl_2$ for 5 days produced an extensive but reversible by 96 hr after dosing hepatic centrolobular loss of glycogen in NC and SH rats. No other hepatic changes were observed in any rats after either $MeCl_2$ injection regimen. No changes were seen in kidneys or hearts. $MeCl_2$ for 5 days did cause vascular congestion and limited atelectasis and pneumonia. | Douglas et al., 1980a |
| $MeCl_2$ | Renal hypertensive (RH) and NC rats given biweekly subcutaneous injections of 0.15 ml/100 g $MeCl_2$ for a total of 15 doses. Rats killed at 24 or 28 wks and histological examination performed of kidneys, lungs, adrenal, and livers. | 11 RH and 3 NC Sprague-Dawley treated rats.<br>2 RH and 11 NC untreated control rats | $MeCl_2$ reduced the systolic blood pressure in the RH rats but had no effect on the blood pressure of the NC rat. Hepatic damage by $MeCl_2$ was so minimal that most results of the histological studies were reported as normal. Lung tissue, where conversion of angiotensin I to II occurred, was not affected by $MeCl_2$ treatment. | Loyte, 1973 |

## REPRODUCTIVE AND TERATOGENICITY STUDIES

### ORAL EXPOSURE

Teratogenicity studies have been conducted with $MeCl_2$ in the drinking water (Bornmann and Loeser, 1967; Clayton and Clayton, 1981; WHO, 1984) and in the feed (Nishio et al., 1984) of rats (Table 9). $MeCl_2$ was not teratogenic in these studies.

### INHALATION EXPOSURE

The potential teratogenicity of $MeCl_2$ by inhalation has been studied in rats (Bornschein et al., 1980; Hardin and Manson, 1980; Heppel et al., 1944; Leong et al., 1975; Schwetz et al., 1975), mice (Leong et al., 1975; Schwetz et al., 1975), rabbits and dogs (Heppel et al., 1944) (Table 9). Generally, $MeCl_2$ was not teratogenic in these studies.

## MUTAGENESIS AND CARCINOGENESIS

### MUTAGENICITY STUDIES

Both positive and negative results have been obtained with $MeCl_2$ in the *Salmonella*/mammalian-microsome mutagenicity test (Ames test) (Andrews et al., 1976; Buijs et al., 1984; Douglas et al., 1980b; Gocke et al., 1981; Gopalan et al., 1980; 1981; Green, 1983; Hughes et al., 1984; Jongen et al., 1978; 1982; 1984; Kanada and Uyeta, 1978; Kirwin et al., 1980; Matsumoto et al, 1981; McCarroll et al., 1983; McGregor, 1979; Nestmann et al., 1980; Osterman-Golkar et al., 1983; Rapson et al., 1980; Simmon, 1977; Simmon et al., 1977) (Table 10). Researchers have used both the standard Ames test (Ames et al., 1975) and modifications of the Ames test, and results seem to

TABLE 9

REPRODUCTIVE AND TERATOGENICITY STUDIES

| $MeCl_2$ Concentration | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| | | | ORAL EXPOSURE | |
| 125 ppm in drinking water | Rats were given $MeCl_2$ in drinking water for 13 weeks before mating. | Unspecified number of Wistar rats | No deleterious effects were observed on the female fertility index, litter size, survival of pups at 4 weeks, and number of resorptions. | Bornmann and Loeser, 1967; Clayton and Clayton, 1981; WHO, 1984 |
| 0.04, 0.4, and 4.0 percent in the diet | Rats were fed $MeCl_2$ in the diet from days 0 to 20 of pregnancy. Fetuses were examined on day 20 and neonatal growth was measured for 8 weeks after birth. | Unspecified number of unspecified strain of rats | Maternal body weight was reduced in the 4.0 percent group. There were no differences in any group in the number of implantations and resorptions. Female fetal weight in the 0.4 percent group was reduced. There were no external malformation observed by fetal skeletal and visceral examination and no differences were observed in any group in the frequency of delayed ossifications or in the dilatation of the renal pelvis. At the 8th wk after birth, postnatal weight gain was reduced in male pups and a reduction in absolute liver weight was observed in the 0.4 percent group males. The researchers stated that no teratogenic effect was observed in rats fed $MeCl_2$ in the diet. | Nishio et al., 1984 |
| | | | INHALATION EXPOSURE | |
| 4500 ppm | Rats were exposed to $MeCl_2$ 12 to 14 days before breeding and during 17 days of gestation. All exposures lasted 6 hr daily. | Two groups of 5 female Long-Evans hooded rats | A higher percentage of resorbed and dead fetuses was observed in the group exposed pregestationally than in the group exposed only during gestation. The researchers stated that results of a larger study (detailed below) did not corroborate these findings. | Hardin and Manson, 1980 |
| 4500 ppm | Groups of rats were exposed to $MeCl_2$ or filtered air 6 hr daily for 21 days before and/or for 17 days during gestation. 20 rats were killed at term for teratologic assessment and measurement of maternal liver weight. 10 rats were allowed to deliver pups and the behavior of the pups was evaluated (Bornschein et al., 1980). Two replicate experiments were performed. | 4 groups of 30 female hooded Long-Evans rats | Maternal hepatic weights were increased and fetal body weights were decreased in the groups exposed to $MeCl_2$ during gestation. Litter effects, in regard to clustering of the incidence of dead and resorbed fetuses were not observed. The sex ratio was not altered. There were no differences in the incidences of gross external skeletal, or soft-tissue anomalies in fetuses in any group. $MeCl_2$ exposure before and during gestation did not affect the incidence of maternal toxicity or embryotoxicity in comparison to gestational exposure alone. The researchers stated that no overt tertogenic or embryotoxic effects were seen following exposure to $MeCl_2$. | Hardin and Manson, 1980 |

TABLE 9 - Continued

REPRODUCTIVE AND TERATOGENICITY STUDIES

| $MeCl_2$ Concentration | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 4500 ppm | Groups of rats were exposed to $MeCl_2$ (probably 6 hr daily) or filtered air for 21 days before and/or for 17 days during gestation. 20 rats per group were killed at term and embryotoxic and teratogenic effects were evaluated (Hardin and Manson, 1980). The other 10 rats per group delivered pups and the behavior of 8 of the pups from each litter was evaluated. Pups were weaned at 21 days and litter size was reduced to 2 males and 2 females. These 4 rats were observed until they were approximately 5 months old. Two replicate experiments were performed. | 4 groups of 30 female hooded Long-Evans rats | Offspring of rats exposed to $MeCl_2$ before and/or during gestation had altered rates of behavioral habituation to novel environments in the absence of overt maternal toxicity, or teratogenicity. Each treatment group had effects that varied with age and behavioral task. Treatment effects were observed when pups were as young as 10 days and as old as 150 days. These effects were observed in male and female mice in pre-weaning test but were not observed in adult female rats. No treatment effects were observed in growth rates, long-term feed and water consumption, wheel running activity, and avoidance learning. | Bornschein et al., 1980 |
| 1100 ppm | Rats were exposed to $MeCl_2$ 8 hr daily, 5 days per week, for 15 weeks. | 16 young rats, unspecified strain | Maternal weight gain was observed and "many" litters were born during the experiment. | Heppel et al., 1944 |
| 5000 ppm (17 mg/l) | Rats were exposed to $MeCl_2$ 7 hr daily, 5 days per week, for up to 132 exposures. | 11 male rats and 1 female rat, unspecified strain | The one female rat died shortly after giving birth to a litter and after 22 $MeCl_2$ exposures. The researchers stated that reproductive function was unimpaired by $MeCl_2$ | Heppel et al., 1944 |
| 1225 ppm | Rats were exposed to $MeCl_2$ 7 hr daily on days 6 to 15 of gestation. Rats were killed on day 21 and livers were removed and weighed. Embryotoxic and teratogenic effects were evaluated. | 20 to 35 female Sprague-Dawley rats and controls | No effect was observed on rat mean body weight or feed consumption. Mean absolute liver weight significantly increased but there was no effect on mean relative liver weight. No effect was observed on the average number of implantation sites per litter, litter size, the incidence of fetal resorptions, fetal sex ratios, and fetal body measurements. The incidence of fetal gross anomalies observed by external examination of treated rats was not different from control rats. The incidence of lumbar ribs or spurs was significantly decreased in exposed rats compared to that of controls and the incidence of delayed ossification of sternebrae was significantly greater than in the controls. No abnormalities of organs, tissues, or cells were observed upon microscopic examination of saggital sections of whole fetuses. The researchers stated that $MeCl_2$ did not cause significant maternal, embryonal, or fetal toxicity and was not teratogenic for rats at the concentration studied. | Leong et al., 1975; Schwetz et al., 1975 |

## TABLE 9 - Continued

### REPRODUCTIVE AND TERATOGENICITY STUDIES

| $MeCl_2$ Concentration | Method | No. and Species of Animal | Results and Comments | References |
|---|---|---|---|---|
| 1225 ppm | Mice were exposed to $MeCl_2$ 7 hr daily on days 6 to 15 of gestation. Mice were killed on day 18 and livers were removed and weighed. Embryotoxic and teratogenic effects were evaluated. | 30 to 40 female Swiss Webster mice and controls | Mean body weight increased significantly. Mean absolute liver weight significantly increased but there was no effect on mean relative liver weight. No effect was observed on the average number of implantation sites per litter, litter size, the incidence of fetal resorptions, fetal sex ratios, and fetal body measurements. The incidence of fetal gross anomalies observed by external examination of exposed mice was not different from control rats. A significant number of litters from exposed mice containing pups with a single extra center of ossification in the sternum. No abnormalities of organs, tissues, or cells were observed upon microscopic examination of saggital sections of whole fetuses. The researchers stated that $MeCl_2$ did not cause significant maternal, embryonal, or fetal toxicity and that it was not teratogenic for mice at the concentration studied. | Leong et al., 1975;<br>Schwetz et al., 1975 |
| 5000 ppm (17 mg/l) | Rabbits were exposed to $MeCl_2$ 7 hr daily, 5 days per week, for a total of 131 exposures. | 2 male and 2 female rabbits | No rabbits died and all appeared "well nourished." Both female bore litters but did not raise them. The researchers stated that this may have been due to the disturbance resulting from daily transfers to the exposure chamber. The researchers also stated that reproductive function was unimpaired by $MeCl_2$. | Heppel et al., 1944 |

TABLE 10

SHORT-TERM TESTS PREDICTIVE OF MUTAGENICITY AND CARCINOGENICITY

| Test | Method | Results | Comments | References |
|---|---|---|---|---|
| Modified Ames test | *S. typhimurium* TA 1535 with and without metabolic activation. Plates incubated in jars and MeCl$^2$ gas was introduced into the jars. | + | $MeCl_2$ was positive in TA1535 to the same degree with and without metabolic activation. | Andrews et al., 1976 |
| Modified Ames test | $MeCl_2$ spot tests with *S. typhimurium* TA 1530 and TA 1535. | - | The researchers stated that $MeCl_2$ was negative probably as a result of its volatility. | Buijs et al., 1984 |
| Ames test | $MeCl_2$ plate incorporation with *S. typhimurium* TA1535, TA100, TA1537, TA1538, and TA98. Metabolic activation probable. | - | - - - | Douglas et al., 1980b |
| Ames test | $MeCl_2$ plate incorporation with *S. typhimurium* TA1535, TA100, TA1537, TA1538, and TA98 with and without metabolic activation. Plates incubated in desiccators. | +/- | $MeCl_2$ was positive in TA100 and TA98 with and without metabolic activation and was negative in the other strains tested. | Gocke et al., 1981 |
| Modified Ames test | $MeCl_2$ spot tests with *S. typhimurium* TA1535, TA100, TA1537, TA1538, TA98, and TA1978. Plates incubated in sealed polythene bags. | ? | $MeCl_2$ induced acute toxicity and, therefore, its mutagenicity could not be ascertained. | Gopalan et al., 1980; 1981 |
| Modified Ames test | *S. typhimurium* TA100 with and without metabolic activation. Plates incubated in air-tight glass jars and $MeCl_2$ vapor introduced into the jars. | + | $MeCl_2$ was positive in TA100 to the same degree with and without metabolic activation. | Green, 1983 |
| Modified Ames test | $MeCl_2$ preincubation. *S. typhimurium* TA100, TA98, and TA97 with and without metabolic activation. | +/- | $MeCl_2$ was positive in TA98 with and without metabolic activation and was negative in the other strains tested. | Hughes et al., 1984 |
| Modified Ames test | *S. typhimurium* TA100 and TA98 with and without metabolic activation. Plates incubated in gas-tight boxes and $MeCl_2$ evaporated in the boxes. | + | $MeCl_2$ was positive in TA100 and TA98 with and without metabolic activation. The mutation rate was related to the dose and increased with metabolic activation. | Jongen et al., 1978; 1982; 1984 |
| Ames test | $MeCl_2$ plate incorporation with *S. typhimurium* TA100 and TA98 with and without metabolic activation. | + | $MeCl_2$ was positive with and without metabolic activation (strain(s) unspecified). The mutation rate was increased with metabolic activation. | Kanada and Uyeta, 1978 |
| Modified Ames test | *S. typhimurium* TA1535, TA100, TA1537, TA1538, and TA98 with and without metabolic activation. Plates incubated in desiccators and $MeCl_2$ gas introduced into the dessicators. | +/- | $MeCl_2$ was mutagenic in TA100 and TA98 and slightly mutagenic in TA1535 with and without activation and was negative in the other strains tested. | Kirwin et al., 1980 |
| Ames test | $MeCl_2$ plate incorporation with *S. typhimurium* TA 100. | + | - - - | Matsumoto et al., 1981 |

TABLE 10 - Continued

SHORT-TERM TESTS PREDICTIVE OF MUTAGENICITY AND CARCINOGENICITY

| Test | Method | Results | Comments | References |
|---|---|---|---|---|
| Modified Ames test | $MeCl_2$ microfluctuation test with S. typhimurium TA1535, TA100, and TA98. Plates incubated in modular incubator chambers and $MeCl_2$ introduced into the chamber. | +/- | $MeCl_2$ was positive in TA1535 and TA100 and was negative in TA98. | McCarrol et al., 1983 |
| Ames test | $MeCl_2$ plate incorporation with S. typhimurium TA1535 and TA100. | + | $MeCl_2$ was mutagenic in TA100 and, to a lesser extent, was mutagenic in TA1535. | McGregor, 1979 |
| Ames test and modified Ames test | Three methods: $MeCl_2$ plate incorporation with S. typhimurium TA1535, TA100, TA1537, TA1538, and TA98 with metabolic activation. Plates incubated outside and within a dessicator. Plates without $MeCl_2$ incorporation incubated in desiccator and $MeCl_2$ was was evaporated in the desiccator. | +/- | $MeCl_2$ was not mutagenic when incorporated into plates and incubated outside or within a dessicator. $MeCl_2$ was mutagenic in TA1535 and TA100 when plates were incubated in a dessicator and $MeCl_2$ was evaporated in the dessicator. | Hestmann et al., 1980 |
| Ames test and modified Ames test | Two methods: $MeCl_2$ plate incorportion with S. typhimurium TA1950, TA1535, and TA100. $MeCl_2$ spot test with plates incubated in a desiccator. | +/- | $MeCl_2$ was mutagenic in TA100 in the plate incorporation test. $MeCl_2$ was mutagenic in TA1950 and TA100 and was not mutagenic in TA1535 in spot test plates incubated in a desiccator. | Osterman-Golkar et al., 1983 |
| Ames test | $MeCl_2$ plate incorporation with S. typhimurium TA100. | - | - - - | Rapson et al., 1980 |
| Modified Ames test | S. typhimurium TA100 with and without metabolic activation. Plates incubated in a desiccator and $MeCl_2$ introduced into the desiccator. | + | $MeCl_2$ was mutagenic in TA100 with and without metabolic activation. | Simmon, 1977;<br>Simmon et al., 1977 |
| Mutation in Bacteria | $MeCl_2$ spot test with Escherichia coli WU361089 $tyr^-$. Plates incubated in desiccator. | + | $MeCl_2$ was positive; the E. coli mutated to tyrosine phototrophy. | Osterman-Golkar et al., 1983 |
| Mutation in Bacteria | $MeCl_2$ spot test with E. coli Sd-4, a streptomycin dependent strain. Plates incubated in desiccator. | - | $MeCl_2$ was negative; the E. coli did not mutate to streptomycin nondependence. | Osterman-Golkar et al., 1983 |
| Prophage induction in Bacteria | $MeCl_2$ spot test with E. coli K-39(λ). Plates incubated in desiccator. | + | - - - | Osterman-Golkar et al., 1983 |
| Rec-assay in Bacteria | Bacillus subtilis | - | - - - | Kanada and Uyeta, 1978 |
| Repair test in Yeast | Repair deficient and non-repair deficient Saccharomyces cerevisiae and Schizosaccharomyces pombe. | - | - - - | Hestmann et al., 1982 |

TABLE 10 - Continued

SHORT-TERM TESTS PREDICTIVE OF MUTAGENICITY AND CARCINOGENICITY

| Test | Method | Results | Comments | References |
|---|---|---|---|---|
| Mitotic Recombination in Yeast | S. cerevisiae D7 and D4 incubated with $MeCl_2$ for 1 or 4 hr. | + | $MeCl_2$ decreased cell survival and induced mitotic gene convertants and recombinants and, to a lesser extent, gene revertants in D7 incubated for 1 hr. A marginal genetic effect was observed with D7 incubated for 4 hr or D4 incubated for 1 or 4 hr. | Callen et al., 1980 |
| Mitotic Recombination in Yeast | S. cerevisiae D3 suspension exposed to $MeC_2$ for 4 hr. | - | - - - | Simmon et al., 1977 |
| Forward mutation test (HGPRT locus) | Chinese hamster V79 and ovary cells exposed to 0.5 to 5 percent (v/v) $MeCl_2$ for 1 hr. | - | $MeCl_2$ was only weakly cytotoxic. | Jongen et al., 1981 |
| DNA Repair Synthesis | Rat hepatocytes incubated with 1 to 30 mM $MeCl_2$ for 3 hr. | - | - - - | Andrae and Wolff, 1983 |
| Inhibition of DNA Synthesis | Chinese hamster ovary cells exposed to 10 to 1000 μg/ml $MeCl_2$ for 20 hr. | - | No detectable toxicity. | Garrett and Lewtas, 1983 |
| Inhibition of DNA Synthesis | Chinese hamster V79 and human fibroblast AN cells exposed to 0.5 to 5 percent $MeCl_2$ for 1 hr. | + | DNA synthesis was inhibited by $MeCl_2$ but recovery of synthesis was observed immediately after removal of the $MeCl_2$. | Jongen et al., 1981 |
| Unscheduled DNA Synthesis | Chinese hamster V79 and human fibroblast AN cells exposed to 0.5 to 5 percent $MeCl_2$ for 1 hr. | - | - - - | Jongen et al., 1981 |
| Inhibition of DNA Synthesis | Human lymphocytes exposed to 2.5 to 10 μl/ml $MeCl_2$ with and without metabolic activation for 4 hr. | - | - - - | Perocco and Prodi, 1981a; 1981b |
| Unscheduled DNA Synthesis | Human lymphocytes exposed to 2.5 to 10 μl/ml $MeCl_2$ with and without metabolic activation for 4 hr. | - | - - - | Perocco and Prodi, 1981a; 1981b |
| Unscheduled DNA Synthesis | Fischer 344 rat and B6C3F1 mouse hepatocytes exposed to 0 to 4000 ppm $MeCl_2$. | - | There was a reproducible but small increase in mean nuclear and mean cytoplasmic counts for mouse hepatocytes. | ICI, 1986c |
| Unscheduled DNA Synthesis | Groups of 8 to 15 Fische 344 rats and B6C3F1 mice were exposed by inhalation to 0 to 4000 ppm $MeCl_2$ for 2 to 6 hr, and then hepatocyte suspensions were prepared. | - | There was a reproducible but small increase in mean nuclear and mean cytoplasmic counts for mouse hepatocytes. There was an elevated percentage of cells in repair, but the mean nett grain counts of these cells were not increased significantly. | ICI, 1986c |
| Scheduled DNA Synthesis (induction of S-phase hepatocytes) | B6C3F1 mice were exposed by inhalation for 2 hr once or twice to 4000 ppm $MeCl_2$ and were injected with radioactive thymidine at various times. Hepatocytes were examined. | + | Small, variable, and statistically significant increases in scheduled DNA synthesis observed. | ICI, 1986d |

TABLE 10 - Continued

SHORT-TERM TESTS PREDICTIVE OF MUTAGENICITY AND CARCINOGENICITY

| Test | Method | Results | Comments | References |
|---|---|---|---|---|
| Binding to rat hepatocyte macromolecules | Rat hepatocytes incubated with 42 mM radioactively labeled $MeCl_2$ for 15 to 60 min. | +/- | A small amount of radioactivity was covalently bound to proteins and lipids. No radioactivity was bound to DNA or RNA. | Cunningham et al., 1981;<br>Sipes and Gandolphi, 1980 |
| Sister chromatid exchange | Chinese hamster V79 cells exposed to 0.5 to 4 percent $MeCl_2$ with and without metabolic activation for 1 to 4 hr. | + | Small but significant increase in sister chromatid exchange at all doses and weak dose-dependency both with and without metabolic activation. | Jongen et al., 1981 |
| Sister chromatid exchange | Chinese hamster ovary cells were exposed to 1.8 to 7 percent $MeCl_2$ for 2 to 24 hr. | +/- | No increase in sister chromatid exchanges after 2 to 10 hr exposures. Dose-related increases were observed after 24 hr exposure to 1.8 to 7 percent $MeCl_2$ but increase was significant only at 7 percent $MeCl_2$. | McCarrol et al., 1983 |
| Sister chromatid exchange | Chinese hamster ovary cells exposed to 2 to 10 µl/ml $MeCl_2$ with and without metabolic activation for 2 hr. | - | $MeCl_2$ did not induce an increase in sister chromatid exchanges but mitotic delay was observed | Thilagar and Kumaroo, 1983 |
| Chromosome aberrations | Chinese hamster ovary cells exposed to 2 to 10 µl/ml $MeCl_2$ with and without metabolic activation for 2 hr. | - | There was a dose-dependent increase in chromosome aberrations. | Thilagar and Kumaroo, 1983 |
| Micronucleus test | Groups of 4 male and female mice given two intraperitoneal doses of 238 to 952 mg/kg $MeCl_2$ in olive oil 24 hr apart. Bone marrow smears prepared at 30 hr. | - | All mice survived to 30 hr. There was no increase in chromosome aberrations in the bone marrow of of treated mice. | Gocke et al., 1981 |
| Micronucleus test | Groups of 5 male and 5 female C57BL/6J/Alpk mice were given 1250 to 4000 ppm/kg $MeCl_2$ in corn oil orally. Bone marrow smears prepared at 24 to 72 hr. | - | - - - | ICI, 1986e |

TABLE 10 - Continued

SHORT-TERM TESTS PREDICTIVE OF MUTAGENICITY AND CARCINOGENICITY

| Test | Method | Results | Comments | References |
|---|---|---|---|---|
| Micronucleus test | Tranescantia paludosa exposed to 0.24 to 18 percent $MeCl_2$ for 6 hr or less. | +/- | At high concentrations, $MeCl_2$ was borderline positive and toxic. The researchers suggested that this result may mean that $MeCl_2$, commonly used as such, is not a suitable extractant for mutagen-testing purposes. | Ma et al., 1984 |
| Cell transformation | Fischer rat embryo cells were exposed to 160 to 1600 mM $MeCl_2$ for 48 hr. Transformed cells were injected subcutaneously into newborn Fischer rats and tumor incidence was determined. | + | $MeCl_2$ induced cell transformation. Transformed cells were injected into rats and undifferentiated fibrosarcomas were produced at the site of inoculation in 5 of 5 rats by 60 days. Non-transformed cells exposed to acetone produced no tumors in 13 rats by 82 days. | Price et al., 1978 |
| Viral transformation of cells | Hamster embryo cells were incubated in a sealed treatment chamber for approximately 20 hr and $MeCl_2$ was evaporated in the chamber (12 to 120 µg/cm$^3$). Adenovirus SA7 was introduced and viral transformation of the cell was determined. | + | The viral transformation frequency was significantly increased in a dose-dependent manner and there was an absolute increase in the number of viral foci. | Hatch et al., 1981; 1982; 1983 |
| Sex Linked Recessive Lethal Mutatations | $MeCl_2$ was given to Drosophila melanogaster in the feed and the X chromosomes were examined in each of three successive broods (3, 3, and 4 days). | + | There was an increased frequency of recessive lethals in the first brood, which represents mature sperm. | Gocke et al., 1981 |

vary primarily with the protocol used. $MeCl_2$ was generally negative in the standard plate incorporation test and was positive when the plates without $MeCl_2$ incorporated in the media were incubated in air-tight chambers, and $MeCl_2$ vapor was introduced into the chambers. The results of some researchers were contrary to this generalization.

$MeCl_2$ has been tested in a variety of other short-term tests predictive of mutagenicity and carcinogenicity, and both positive and negative results have been obtained (Andrae and Wolff, 1983; Callen et al., 1980; Cunningham et al, 1981; Garrett and Lewtas, 1983; Gocke et al., 1981; Hatch et al., 1981; 1982; 1983; ICI, 1986c; 1986d; 1986e; Jongen et al., 1981; Kanada and Uyeta, 1978; Ma et al., 1984; McCarroll et al., 1983; Nestmann et al., 1982; Osterman-Golkar et al., 1983; Perocco and Prodi, 1981a; 1981b; Price et al., 1978; Simmon et al., 1977; Sipes and Gandolfi, 1980; Thilagar and Kumaroo, 1983).

$MeCl_2$ has been used frequently as an extractant for testing agents for mutagenicity. Positive results in some mutagenicity tests suggest that $MeCl_2$ may not be ideal for this purpose.

A study, in which rats inhaled $MeCl_2$ and bone marrow was examined for cytogenetic aberrations, is described in the section on carcinogencity (Burek et al., 1984).

## CARCINOGENICITY STUDIES

### ORAL STUDIES

The National Coffee Associaton [NCA] (1982; 1983) has sponsored carcinogenicity studies in which $MeCl_2$ was administered in the drinking water of Fischer 344 albino rats and $B6C3F_1$ mice for 24 months (Table 11).

TABLE 11

CARCINOGENICITY STUDIES

| Material and Conc. or Dose Tested | Method | *Results and Comments | Reference |
|---|---|---|---|
| | | ORAL STUDIES | |
| 0, 5, 125, and 250 mg/kg/day $MeCl_2$ in the drinking water | Groups of 85 male and 85 female Fischer 344 rats were given $MeCl_2$ in the drinking water for 24 mos. A recovery group of 25 male and 25 female rats received 250 mg/kg/day $MeCl_2$ for 78 weeks and then only water for the remainder of the study. Two control groups consisted of 85 and 50 rats of each each sex, respectively. All animals were necropsied. | The researchers stated that under the conditions of this study, $MeCl_2$ was not carcinogenic for rats. They observed a no-effect $MeCl_2$ concentration for toxicological and non-neoplastic histopathological effects at 5 mg/kg/day. | NCA, 1982; Serota et al., 1986a |
| 0, 60, 125, 185, and 250 mg/kg/day $MeCl_2$ in the drinking water | Groups of 100 to 200 male and 50 to 100 female $B6C3F_1$ mice were given $MeCl_2$ in the drinking water for 24 mos. Two control groups consisted of 50 to 65 mice of each sex. All animals were necropsied. | The researchers stated that under the conditions of this study, $MeCl_2$ was not carcinogenic for mice. They observed a no-effect $MeCl_2$ concentration for toxicological and non-neoplastic histopathological effects at 185 mg/kg/day. | NCA, 1983; Serota et al., 1986b |
| $MeCl_2$ in corn oil | $MeCl_2$ was administered by gavage to rats and mice for 2 years. | Due to discrepancies in the experimental data, the draft report will not be issued as a final report. However, a marginal but significant increase in the number of lung tumors in female mice was observed following $MeCl_2$ administration. | NTP, 1986 |
| 6 percent coffee, decaffeinated with $MeCl_2$, in the feed | Coffee, decaffeinated with $MeCl_2$, was given in the feed to several groups of male and female rats for 2 years. A control group received feed alone. 65 to 74 rats per group were necropsied. | There was no significant increase in the incidence of neoplasms when rats were given coffee, decaffeinated with $MeCl_2$, in the feed. | Wurzner et al., 1977 |
| | | INHALATION STUDIES | |
| 0, 1000, 2000, and 4000 ppm $MeCl_2$ | Groups of 50 F344/N rats of each sex were exposed to $MeCl_2$ by inhalation 6 hr a day, 5 days a week for 102 weeks. Necropsies were performed on all rats. | NTP concluded that there was "some evidence of carcinogenicity" of $MeCl_2$ for female F344/N rats, as indicated by increased incidences of mammary gland neoplasms. | NTP, 1986 |
| 0, 2000, and 4000 ppm $MeCl_2$ | Groups of 50 $B6C3F_1$ mice of each sex were exposed to $MeCl_2$ by inhalation 6 hr a day, 5 days a week for 102 weeks. Necropsies were performed on all mice. | NTP concluded that there was "clear evidence of carcinogenicity" of $MeCl_2$ for male and female $B6C3F_1$ mice, as indicated by increased incidences of alveolar/bronchiolar and hepatocellular neoplasms. | NTP, 1986 |

TABLE 11 - Continued

CARCINOGENICITY STUDIES

| Material and Conc. or Dose Tested | Method | *Results and Comments | Reference |
|---|---|---|---|
| 0, 500, 1500, and 3500 ppm $MeCl_2$ | Groups of 129 Sprague-Dawley rats of each sex were exposed to $MeCl_2$ by inhalation 6 hr a day, 5 days a week excluding holidays for 2 years. Necropsies were performed. | The researchers did not conclude that $MeCl_2$ was carcinogenic to rats. | Burek et al., 1984; Rampy et al., 1979; Reznik, 1984 |
| 0, 500, 1500, and 3500 ppm $MeCl_2$ | Groups of 107 to 109 Golden Syrian hamsters were exposed to $MeCl_2$ by inhalation 6 hr a day, 5 days a week excluding holidays for 2 years. Necropsies were performed. | The researchers did not conclude that $MeCl_2$ was carcinogenic to hamsters. | Burek et al., 1984; Rampy et al., 1979; Reznik, 1984 |
| 0, 50, 200, and 500 ppm $MeCl_2$ | Groups of 90 Sprague-Dawley rats were exposed to 0 to 500 ppm $MeCl_2$ by inhalation 6 hr a day, 5 days a week excluding holidays for 20 (male rats) or 24 (female rats). Two groups of 30 female rats were exposed to 500 ppm $MeCl_2$ only for the first 12 mo of the study or only for the second 12 mo of the study. All rats were necropsied. | The researchers concluded that exposure of rats to 500 ppm $MeCl_2$ resulted in minimal hepatic changes and benign mammary tumors in female rats. Exposure to 200 ppm $MeCl_2$ resulted in an equivocal increase in the percentage of rats with multinucleated hepatocytes. There was no indication of a toxicologic response following exposure of rats to 50 ppm $MeCl_2$. | Nitschke et al., 1982 |
| | | INTRAPERITONEAL STUDY | |
| 160, 400, and 800 mg/kg $MeCl_2$ in Tricapyrin | $MeCl_2$ was injected intraperitoneally three times a week for a total of 16 to 17 injections into groups of 20 A/St male mice. | There was a positive trend in the incidence of pulmonary adenomas in treated mice and the response at the 160 mg/kg dose was almost significant. The researchers suggested that $MeCl_2$ might be carcinogenic in a large-scale test. | Theiss et al., 1977 |

*More complete results detailed in the text.

Groups of 85 male and 85 female Fischer 344 rats received $MeCl_2$ at target concentrations of 5, 50, 125, and 250 mg/kg/day in deionized drinking water (NCA, 1982; Serota et al., 1986a). A "recovery" group of 25 male and 25 female rats received 250 mg/kg/day $MeCl_2$ for 78 weeks and then received only deionized water for the remainder of the study. Two control groups of 84 and 50 animals of each sex, respectively, received only deionized drinking water. The study was conducted in a laminar airflow room design. Some rats from the larger control group and all the treatment groups except the recovery group were killed by intraperitoneal administration of a barbiturate during the study; 5 of each sex were killed at 26 weeks, 10 of each sex at 52 weeks, and 20 of each sex at 78 weeks. All remaining rats were killed at 104 weeks. These animals and all those found dead or moribund were necropsied. Survival, body weight gains, total feed consumption during the first 13 weeks of the study, water consumption, clinical laboratory findings including hematology, clinical chemistry, and urinalysis parameters, ophthalmoscopic findings, the results of clinical pathology studies, absolute and relative organ weights, and the results of gross and microscopic examination were reported.

The administration of $MeCl_2$ in the drinking water had no effect on survival, clinical appearance, ophthalmoscopic findings, necropsy findings and organ weights in rats (NCA, 1982; Serota et al., 1986a). Significantly smaller body weight gains and reduced water consumption, as well as a decrease in feed consumption, were observed during the study in the recovery groups and in the groups of rats given 125 and 250 mg/kg/day $MeCl_2$ in the drinking water. These investigators believed these effects were interrelated and attributed them to the administration of $MeCl_2$. $MeCl_2$-related increases in mean hematocrit, hemoglobin, and erythrocyte counts were observed in both male and female rats given 50, 125, and 250 mg/kg/day $MeCl_2$; the investigators stated that these increases may be due to hypoxia or to a decrease in plasma volume resulting from reduced water consumption. $MeCl_2$-related and dose-dependent decreases were observed in serum alkaline phosphatase, creatinine, blood urea nitrogen, total protein, and serum cholesterol values in both sexes of the higher-dose groups but the decreases were of low magnitude, and most of the data were within the range of Fischer 344 rat historical control data for the laboratory. Therefore, the researchers did not believe that these effects had any long-term biological significance. An increased incidence of foci/areas of cellular alteration was observed in the livers of male and female rats given 50, 125, and 250 mg/kg/day $MeCl_2$ in the drinking water for 104 weeks and in those given 250 mg/kg/day for 78 weeks; the increased incidence was noted at 78 weeks and at the end of the study. There was an increased incidence of hepatic fatty change in the 2 higher-dose groups at 78 and 104 weeks. There was a decreased severity of hepatic fatty change in the recovery groups at 104 weeks in comparison to the group that received 250 mg/kg/day for the entire study; this may suggest a regression of this effect. The researchers stated that under the conditions of this study, $MeCl_2$ was not carcinogenic for rats. They observed a no-effect $MeCl_2$ concentration for toxicological and non-neoplastic histopathological effects at 5 mg/kg/day.

Groups of 100 to 200 male and 50 to 100 female $B6C3F_1$ mice received $MeCl_2$ at targeted concentration of 60, 125, 185, and 250 mg/kg/day in deionized drinking water (NCA, 1983; Serota et al., 1986b). Two control groups of 50 to 65 animals of each sex received only deionized drinking water. The study was conducted in a laminar airflow room design. Animals found dead or moribund during the study were necropsied. At the termination of the study at 104 weeks, the remaining mice were anesthetized, killed by exsanguination, and necropsied. Survival, body weight changes, water consumption, clinical signs, including palpable tissue masses, total and differential leukocyte counts and the results of gross and microscopic studies were reported.

The administration of $MeCl_2$ in the drinking water had no effect on survival of male mice, clinical signs, body weight changes, water consumption, and necropsy findings (NCA, 1983; Serota et al., 1986b). There was a significant negative linear trend for female mouse mortality data, and several instances of significantly higher survival were observed in the $MeCl_2$-exposed groups. Mean leukocyte count was increased significantly in high-dose male and female mice at 52 weeks but not at 104 weeks; the researchers stated that the increase might have been due to $MeCl_2$ administration, but the response was transitory and had little long-term significance. $MeCl_2$-related histomorphologic changes were observed in the livers of mice; there was a marginal increase in the Oil Red O positive material in the liver of the mice that received 250 mg/kg/day $MeCl_2$ in the drinking water. There were no other $MeCl_2$-related non-neoplastic or neoplastic histomorphologic findings. A slight increase in proliferative hepatocellular lesions, adenoma, and carcinoma was observed in treated male mice, but this response was within the range of $B6C3F_1$ mouse historical control data for the laboratory and that reported in the scientific literature. Positive significance for trend was not observed, and positive significance for group comparisons was observed in only 1 case. The researchers did not attribute the observed response to administration of $MeCl_2$. They stated that under the conditions of the study, $MeCl_2$ was not carcinogenic for mice. They observed a no-effect $MeCl_2$ concentration for toxicological and non-neoplastic histopathological effects at 185 mg/kg/day.

The National Toxicology Program (NTP) conducted a 2-year carcinogenicity study, in which $MeCl_2$ was administered in corn oil by gavage to rats and mice. The draft report of this study will not be issued as a final report due to discrepancies in experimental data that compromise a clear interpretation (Federal Register, 1983; EPA, 1985a). However, a marginal but significant increase in the number of lung tumors in female mice was observed following the administration by gavage of $MeCl_2$ in corn oil (NTP, 1986) (Table 11).

Coffee, from which caffeine had been removed by extraction with $MeCl_2$, was given at the maximum tolerated dose of 6% to 7 groups of male and female rats in the feed for 2 years (Wurzner et al., 1977). Three of these groups also received caffeine in the feed. A control group received the feed alone. Rats were killed and examined at 3 and 12 months and at the termination of the experiment. The number of animals necropsied per group ranged from 65 to 74. In comparison with the control group, there was no significant increase in the incidence of neoplasms when the rats were fed coffee decaffeinated with $MeCl_2$ (Table 11).

## INHALATION STUDIES

The NTP (1986) has issued a report that describes the experimental designs, results, and conclusions of single exposure, 19-day repeated exposure, 13-week exposure, and 2-year $MeCl_2$ inhalation studies with male and female F344/N rats and $B6C3F_1$ mice. The single exposure, 19-day repeated exposure, and 13-week exposure inhalation studies are described in the sections on acute toxicity under inhalation studies. The 13-week studies were used to determine the appropriate exposure concentrations for the 2-year studies.

A 4000 ppm concentration of $MeCl_2$ was selected as the maximum exposure concentration for rats in the 2-year studies because of the minimal severity of the histopathologic changes noted after exposure to approximately 4000 ppm $MeCl_2$ for 13 weeks.

Concentrations of 2000 and 4000 ppm $MeCl_2$ were selected for the 2-year mouse studies based on the deaths observed at 8400 ppm $MeCl_2$ and on the severity of histologic changes observed at approximately 4000 ppm $MeCl_2$.

For the 2-year studies, 50 rats of each sex were exposed to 0, 1000, 2000, and 4000 ppm $MeCl_2$ 6 hours a day, 5 days a week for 102 weeks (NTP, 1986). Groups of 50 mice of each sex were exposed to 0, 2000, and 4000 ppm $MeCl_2$ on the same schedule. Necropsies were performed on all the animals. Gross lesions and tissue masses, regional lymph nodes, tracheobronchial lymph nodes, mandibular lymph nodes, salivary glands, sternebrae including marrow, thyroid gland, parathyroid glands, larynges, small intestine, colon, duodenum, liver, heart, trachea, prostates/testes or ovaries/uteri, lungs and mainstream bronchi, skin, gallbladder (only in mice), kidneys, and spleen were examined microscopically.

The mean body weights of treated and control rats were comparable throughout the 2-year $MeCl_2$ inhalation study (NTP, 1986). During exposure to 4000 ppm $MeCl_2$, rats were restless and pawed at their eyes and muzzles. After week 100, survival of female rats exposed to 4000 ppm $MeCl_2$ was significantly less than that of the controls. No other significant differences in survival between any groups of either sex were observed. Survival of male rats was low; survival ranged from 18 to 34%, and most of the deaths occurred during the last 16 weeks of the study. There were significant positive trends in the incidences of mammary gland fibroadenomas in male and female rats. The incidences in males exposed to 4000 pppm $MeCl_2$ and in treated females were significantly greater than those in the control rats. There were also significant trends in the incidences of subcutaneous fibromas and combined fibromas and sarcomas in male rats, but the incidences in the treated rats were not greater than the incidences in the control rats. When subcutaneous neoplasms and mammary gland neoplasms were combined, the incidence of neoplasms in male rats had a significant positive trend, and the incidence in the male rats exposed to 4000 ppm $MeCl_2$ was significantly greater than that in the control rats. Increased incidences of hemosiderosis, hepatocytomegaly, cytoplasmic vacuolization, and necrosis were observed in the livers of treated male and female rats. Bile duct fibrosis was observed in an increased incidence in all treated male rats and in mid dose female rats. A significant positive trend by the life table test was observed in the incidences of hepatic neoplastic nodules and combined neoplastic nodules and hepatocellular carcinomas in female rats; the incidence in the females exposed to 4000 ppm $MeCl_2$ was not significantly greater than that in the control rats. Mesotheliomas of the tunica vaginalis or multiple organs occurred with a significant positive trend in male rats; the incidences in the high dose and mid-dose groups were significantly greater than those in the control rats. A significant positive trend by the life table test was observed in the occurrence of mononuclear leukemia in male and female rats. The incidences in mid-dose and high dose female rats were significantly greater than in the control rats by the life table test. The incidence in the male rats exposed to 1000 ppm $MeCl_2$ was significantly less than that in the control rats. Leukemia may have contributed to the early deaths in the male rats and the reduced survival in the female rats exposed to 4000 ppm $MeCl_2$. In comparison with the incidences in the control rats, the incidences of adrenal gland pheochromocytomas and interstitial cell tumors of the testes in male rats, and combined pituitary gland adenomas and carcinomas in male and female rats were marginally significantly increased; the trend was significant, but there was no significant pairwise difference or the pairwise difference was significant only by life table analysis or there was a significant effect at the low dose, but no significant trend or effect at the high dose. Squamous metaplasia of the nasal cavity was observed in an increased incidence in female rats exposed to 4000 ppm $MeCl_2$. Degeneration of renal tubules was observed in increased incidences in mid dose male rats and in female rats exposed to 4000 $MeCl_2$. Splenic fibrosis was observed in increased incidences in treated male and female rats. In treated male rats, suppurative inflammation of the prostate and hyperplasia of the parathyroid gland were observed in increased incidences. There was no evidence in either sex of $MeCl_2$-related effects on the salivary glands.

The NTP (1986) has concluded that in the 2-year inhalaton study, there was "some evidence of carcinogenicity" of $MeCl_2$ for female F344/N rats, as shown by increased incidences of mammary gland neoplasms.

The mean body weight of the mice exposed to 4000 ppm $MeCl_2$ in the 2-year inhalation study was generally comparable to that of the control mice until week 90, and then was lower than that of the control mice (NTP, 1986). Hyperactivity was observed during exposure of female mice to 4000 ppm $MeCl_2$; it was observed to a lesser extent in male mice exposed to 4000 ppm $MeCl_2$ and in female mice exposed to 2000 ppm $MeCl_2$. During the second year of the study, lethargy was observed in the high dose female rats. The survival of treated male mice was significantly lower than the survival of control mice, and the survival of the high dose group was signficantly lower than that of the low dose group. The survival of the high dose group of female mice was significantly lower than the survival of the low dose group and the control mice. Total deaths increased in a dose-related manner during the last 16 weeks of the study. Significant positive trends were observed in the occurrence of alveolar/bronchiolar adenomas, alveolar/bronchiolar carcinomas, and combined alveolar/bronchiolar adenomas and carcinomas in male and female mice, and the incidences in the treated mice were significantly greater than those in the control mice. The number of mice with multiple lung tumors increased in a dose-related manner. Degeneration of the liver was observed in increased incidences in male mice exposed to 4000 ppm $MeCl_2$ and in all treated female mice. The incidences of hepatocellular adenomas, hepatocellular carcinomas, and combined hepatocellular adenomas and carcinomas occurred with significant positive trends in male and female mice. The incidences of hepatocellular adenomas in male and female mice exposed to 4000 ppm $MeCl_2$, hepatocellular carcinomas in male mice exposed to 4000 ppm $MeCl_2$ and in all treated female mice, hepatocellular adenomas and combined hepatocellular adenomas and carcinomas in treated male mice, and combined hepatocellular adenomas and carcinomas in treated female mice were significantly greater than the incidences in the control mice. The incidences of multiple hepatocellular tumors in mice was dose-related. Significant positive trends by the life table test were observed in the incidences of hemangiosarcomas and combined hemangiomas and hemangiosarcomas in male mice; the incidences in the treated mice were significantly greater by life table pairwise comparisons than those in the control mice. Testicular atrophy was observed in increased incidences in treated male mice. Ovarian atrophy was observed in increased incidences in treated female mice. Uterine atrophy was observed in an increased incidence in female mice exposed to 4000 ppm $MeCl_2$. The testicular, ovarian, and uterine changes may be due to the direct effects of $MeCl_2$ or may be secondary to the pulmonary and hepatic neoplasia induced by $MeCl_2$. The incidence of renal tubule casts and atrophy of splenic follicles was increased in male mice exposed to 4000 ppm $MeCl_2$. Dilatation of the stomach was observed in increased incidences in male and female mice exposed to 4000 ppm $MeCl_2$. There was no evidence in either sex of $MeCl_2$-related effects on the salivary glands.

The NTP (1986) concluded that in the 2-year inhalation study, there was "clear evidence of carcinogenicity" of $MeCl_2$ for male and female $B6C3F_1$ mice, as indicated by increased incidences of alveolar/bronchiolar and hepatocellular neoplasms.

Groups of 129 Sprague-Dawley rats of each sex and groups of 107 to 109 Golden Syrian hamsters of each sex were exposed to 0, 500, 1500, and 3500 ppm $MeCl_2$ 6 hours a day, 5 days a week excluding holidays, for 2 years (Burek et al., 1984; Rampy et al., 1979). Rats were killed at 6, 12, 15, and 18 months and at the termination of the study. Hamsters were killed at 6, 12 and 18 months and at the end of the study. Necropsies and urinalyses were performed, and blood samples were taken for hematology studies and clinical chemistries. Bone marrow from rats was sampled at 6 months for cytogenetic studies (Table 11).

There was a slight decrease in the physical activity of rats exposed to 3500 ppm $MeCl_2$ during the first week only (Burek et al., 1984). No other $MeCl_2$-related effects on the behavior of the rats were observed. A disease consistent with the transient viral infection, sialodacryoadenitis, was observed in male and female rats during the first 2 months of the study; there was no increase in mortality, and all the groups were affected to the same degree. Significantly increased mortality that appeared to be related to exposure was observed in female rats exposed to 3500 ppm $MeCl_2$ during months 18 to 21 of the study. There were no other $MeCl_2$-related effects on survival. There were no exposure-related effects on the body weights of males or females. The mean liver weights of rats exposed to 3500 ppm $MeCl_2$ were increased at 18 months. Both absolute and relative mean liver weights in males and relative mean liver weights in females were increased significantly. The absolute mean liver weight in females was increased, but this was not statistically significant. No other absolute or relative organ weight changes related to $MeCl_2$ exposure were observed. At 15 months, the mean corpuscular volume and mean corpuscular hemoglobin values were significantly increased in all male rats exposed to $MeCl_2$; these values were increased but not significantly in exposed male and female rats in comparison with control rats. No $MeCl_2$-related effects on clinical chemistry or urinalysis values were observed.

An increased number of cytogenetic aberrations was not observed in the bone marrow of rats exposed to $MeCl_2$ by inhalation for 6 months (Burek et al., 1984).

At 12 months, effects on the liver were observed in all treated male and female rats; there was dose-dependent increased hepatocellular vacuolization consistent with fatty change (Burek et al., 1984; Rampy et al., 1979). Large multinucleated hepatocytes with an increased number of large mitochondria with intramitochondrial inclusions were observed in control and treated female rats; the number of these cells was increased significantly in treated rats, but the number and severity were not dose-dependent. A significant increase in the number of foci and areas of altered hepatocytes was observed in females exposed to 3500 ppm $MeCl_2$; no increases were observed in other groups of female rats or in male rats. Foci and areas of altered hepatocytes were apparent after 12 months of exposure to $MeCl_2$, and the number and size increased during exposure. An increased incidence of neoplastic nodules or hepatocellular carcinoma was not observed in any group of rats. There was an increased incidence of individual hepatocellular necrosis in male rats exposed to 1500 and 3500 ppm $MeCl_2$, and there was a slight increase in the number of cases of coagulation necrosis in females exposed to 3500 ppm $MeCl_2$. At 12 months, in comparison with control rats, females exposed to 500, 1500, and 3500 ppm $MeCl_2$ and males exposed to 1500 and 3500 ppm had slightly more hemosiderin pigment in the liver. Female rats exposed to 3500 ppm $MeCl_2$ had a decreased incidence of, and male rats exposed to 1500 and 3500 ppm $MeCl_2$ had decreased severity of, spontaneously occurring age-associated chronic renal disease when compared to control rats. Non-renal lesions that normally occur secondarily in rats with severe renal disease were also reduced in males exposed to 3500 ppm $MeCl_2$. A statistically significant decrease was observed in the incidence of grossly and histologically observed pancreatic nodules in male rats exposed to 1500 and 3500 ppm $MeCl_2$. Male rats exposed to 3500 ppm $MeCl_2$ had a significant increase in the total number of cases of increased extramedullary hematopoiesis in the spleen. There was a significant decrease in the number of male and female rats exposed to 3500 ppm $MeCl_2$ with hemosiderin pigment in the spleen. There was an increased number of benign mammary tumors per tumor-bearing treated female rat. The total number of female rats with benign mammary tumors was not significantly increased in any group, although the total number did increase in an exposure-related manner. Benign mammary tumors were also observed in male rats but were of lower incidence than in female rats. There was an increase, although it was not significant, in the number of benign mammary tumors in male rats exposed to 3500 ppm $MeCl_2$, and there was a slight increase in the total number of benign mammary tumors in male rats exposed to 1500 and 3500 ppm $MeCl_2$; effects in male rats exposed to 1500 and 3500 ppm $MeCl_2$ were dose-dependent. An increased number or incidence of malignant mammary tumors in male and female rats was not observed. Thus, there was no indication of a progression of benign to malignant mammary tumors. Exposure to 3500 ppm $MeCl_2$ reduced the survival of female rats in comparison with the control rats during the final 6 months of the study. This was probably due to the numerous benign mammary tumors in this group. The tumors were benign but were often large and often became ulcerated. Sprague-Dawley rats have a predisposition towards benign mammary tumors. With exposure to $MeCl_2$, an increased number of sarcomas in and around the salivary glands of male rats was observed. The researchers feel that the relevance of the increased incidence of sarcomas in the salivary gland region is uncertain. The rats in the study did have a common viral disease, sialodacryoadenitis, early in the treatment period; the responsible virus affects primarily the salivary glands and was present in both control and treated rats. There appeared to be a dose-related decrease in pituitary tumors in treated female rats.

No treatment-related effect was observed on the upper respiratory tract, including the nasal turbinates, of rats (Reznik, 1984). The cumulative number of all neoplasms, either benign or malignant, was not different in control or exposed female rats (Burek et al., 1985). The researchers did not conclude that $MeCl_2$ was carcinogenic to rats (Reznik, 1984).

There were no $MeCl_2$-related effects on the behavior, the survival, or the body weights of either sex of hamsters (Burek et al., 1984). No $MeCl_2$ exposure-related effects were observed on the mean fasted body weights and mean organ weights of either male or female hamsters. There were possible exposure-related trends in the packed cell volume and hemoglobin concentration values of male and female hamsters but only a few of the mean group values were significant. No $MeCl_2$-related effects on clinical chemistry of urinalysis values were observed.

All hamsters had an increased quantity of hemosiderin pigment in the liver; there was a slight $MeCl_2$ exposure-related effect in male hamsters but not in female hamsters exposed to 3500 ppm $MeCl_2$ for 6 or 12 months (Burek et al., 1984). The toxicological significance of increased hemosiderin is unclear. Amyloid deposits in multiple organs, common in control hamsters, particularly females, were fewer and less severe in hamsters exposed to $MeCl_2$. Control hamsters with severe amyloidosis had secondary lesions and these were also reduced in $MeCl_2$-exposed hamsters, probably because of the decreased severity of amyloidosis. Mortality was less in female hamsters exposed to 1500 and 3500 ppm $MeCl_2$; this appeared to be related to the decreased incidence and severity of amyloidosis in exposed hamsters in comparison to control hamsters. Both male and female hamsters exposed to $MeCl_2$ had fewer biliary cysts in the liver. Male hamsters exposed to 3500 ppm $MeCl_2$ had decreased mineral deposits in the renal cortex and medulla. Increased mineral deposits in the kidneys were observed in all exposed female hamsters. The significance of these findings is unclear. Increased hemosiderin pigment was observed in the adrenals of all exposed male hamsters and of female hamsters exposed to 1500 and 3500 ppm $MeCl_2$. All exposed male hamsters had an increased number of small hyperplastic foci in the adrenal cortex.

No treatment-related effect was observed on the upper respiratory tract, including the nasal turbinates, of hamsters (Reznik, 1984).

There was no $MeCl_2$ exposure-related difference observed in male hamsters in the total number of animals with neoplasms, the total number with benign neoplasms, and the total number with malignant neoplasms (Burek et al., 1984). There was a significant increase in benign neoplasms in female hamsters exposed to 3500 ppm $MeCl_2$, but this was considered to be secondary to the increased survival of this group. The researchers did not conclude that $MeCl_2$ was carcinogenic to hamsters (Reznik, 1984).

Groups of 90 Sprague-Dawley rats were exposed to 0, 50, 200, and 500 ppm $MeCl_2$ by inhalation (Nitschke et al., 1982). The rats were exposed for 6 hours a day, 5 days a week excluding holidays. Total exposure period was 20 months for male rats and 24 months for female rats. Five rats of each sex in each group were killed at 6, 12, 15, and 18 months and were necropsied. Two additional groups of 30 female rats were exposed to 500 ppm $MeCl_2$ only for the first 12 months of the study or only for the second 12 months of the study; 5 rats from each group were killed and necropsied at 18 months. All rats that were moribund and killed or that died during the study were necropsied. Survivors were killed and necropsied at the termination of the study. All tissues were examined histologically. During the study, rats were observed for signs of toxicity and changes in demeanor and appearance, and blood was sampled for clinical determinations (Table 11).

An extra 18 female rats were included in each exposure group and 4 rats each were used at 6, 9, and 12 months to determine the rate of radioactive thymidine incorporation into hepatic DNA (Nitschke et al., 1982). The data at 9 months was lost. These additional rats were not used in any other part of the study.

No treatment-related effects were observed on the behavior of the rats (Nitschke et al., 1982). Signs suggesting infection with sialodacryoadenitis virus were observed in all the rats 2 months after the beginning of the study; all rats were equally affected, and 3 weeks later, the signs had disappeared. The mortality rate of $MeCl_2$-treated rats, except for the females treated only for 12 months, was not different from that of the controls. The mortality rate of the 12 month-treated females was less than that of the controls; according to the investigators, this was probably a chance occurrence. Mortality was high in all groups of male rats, and therefore, the male rat exposure period was shorter than that for the female rats. Within 90 days of the beginning of the study, the mean body weights of all groups of male rats were comparable, and after 70 days, no significant differences were observed in the mean body weights of male rats. The mean body weights of treated female rats were significantly greater than those of the controls throughout most of the exposure period; according to the researchers, this result was a reflection of biological variability. Absolute and relative organ weights of male rats were not affected by $MeCl_2$ treatment. Significant decreases in relative brain and heart weights and significant increases in absolute liver and kidney weights were observed in all treated female rats and were always associated with elevated body weights; according to the researchers, these results were due to elevated body weights and were not a reflection of toxicity. Other differences in absolute and relative organ weights were considered to be spontaneous in nature. Statistically significant differences observed in the clinical chemistry values of treated male rats did not follow a dose-response relationship and/or no consistent trend was noted between scheduled necropsies. No effect was observed on the plasma hormone concentrations of male rats exposed to $MeCl_2$. There was no consistent trend in clinical chemistry values at scheduled necropsies of female rats, but the triglyceride concentrations of female rats exposed to 200 and 500 ppm $MeCl_2$ were elevated at 18 months, and there was a dose-response relationship. A similar increase in triglyceride concentration was not observed at 15 or 24 months, and the increase at 18 months was probably not due to $MeCl_2$. Plasma estradiol concentrations were elevated in exposed female rats at 18 months but were not different from the controls at 12, 15, and 24 months. The researchers believed that the increase at 18 months was not due to $MeCl_2$ exposure. Plasma follicle-stimulating hormone and luteinizing hormone concentrations were unaffected by $MeCl_2$ exposure. Exposure of female rats for 6 or 12 months to $MeCl_2$ did not affect thymidine incorporation into hepatic DNA; there were no detectable alterations in hepatic DNA synthesis or cell turnover.

Rats were examined monthly from month 11 to the termination of the study for palpable masses (Nitschke et al., 1982). The incidence of $MeCl_2$ exposed male rats with palpable masses or in the total number of palpable masses in exposed male rats was significantly greater from that in controls. There was a trend towards increased number of palpable masses in female rats exposed to 500 ppm $MeCl_2$ for 12 months, and there was a statistically significant increase in percentage and/or total number of palpable masses in exposed females after 15 months and from 20 months onward. There was a slight increase in total number of palpable masses in female rats exposed to 50 or 200 ppm $MeCl_2$ for 18 months; the increases were statistically significant at 23 months. Female rats exposed to 500 ppm for only the first 12 months of the study had a higher percentage and a higher number of palpable masses at 21 months than the rats exposed to 500 ppm ~~$MeCl_2$ for the~~ entire study; this was probably due to the increased survival of the former. Female rats exposed to 500 ppm $MeCl_2$ for only the second 12 months of the study had a higher percentage and a higher number of palpable masses after 11 months of exposure than the control group.

There were no definite $MeCl_2$-related gross or histopathologic findings in any rats in the 20 to 24 month treatment groups at any of the interim sacrifices (Nitschke et al., 1982). An apparent trend for a $MeCl_2$-related lesion, a focus or foci of altered cells in the liver, was observed in female rats exposed for 15 months, but this trend was not apparent in female rats at the 6, 12, or 18 month sacrifices or in rats that died or were killed when moribund during the study or were killed at the termination of the study; the researchers believed the apparent dose-response relationship at 15 months was due to biological variability. Hepatocellular vacuolization was observed in most of the rats at each interim sacrifice, but no definite increase with exposure was noted; the researchers stated that these results were due to the small number of rats in each group and to normal variability.

No gross nonneoplastic lesions considered to be the result of $MeCl_2$ inhalation were observed in rats in the 20 to 24 month treatment groups that were killed when moribund or that died spontaneously during the study or in rats that were killed at the termination of the study (Nitschke et al., 1982). An increased incidence of multinucleated hepatocytes was observed in female rats exposed to 500 ppm $MeCl_2$. The biological significance of multinucleated hepatocytes is unknown. The percentage of female rats with multinucleated hepatocytes in the 200 ppm $MeCl_2$-treated group was slightly increased; the researchers called this finding equivocal and could not determine whether it was due to $MeCl_2$ exposure or to normal biological variability. Vacuolization of hepatocytes was seen in many rats, including controls; these were usually very slight in degree and multifocal in distribution. Hepatocellular vacuolization in male rats did not appear to be increased by inhalation of $MeCl_2$. The number of female rats in the 500 ppm $MeCl_2$ group with hepatocellular vacuolization was increased; the researchers stated that this result was of minimal toxicological significance. There was no increase in the hepatocellular vacuolization cumulative incidence or severity in male and female rats exposed to 50 or 200 ppm $MeCl_2$. At the terminal sacrifice of the female rats exposed to 500 ppm $MeCl_2$, there was a statistically significant increase in the number of rats with foci of altered hepatocytes. There was also a significant increase in the incidence of foci of altered hepatocytes in male rats exposed to 200 or 500 ppm $MeCl_2$ at the end of the study. However, neither of these results were significant when data from male and female rats that died during the study were combined with the data from the rats that were killed at the end of the study. The researchers stated that the results observed at terminal sacrifice were due to chance occurrence or biological variability. All other nonneoplastic lesions observed in this study were considered to be spontaneous changes not due to $MeCl_2$ exposure.

The percentage of female rats in the 24 month treatment groups with benign mammary tumors, including adenomas, fibroadenomas, and fibromas, increased in a dose-dependent manner with $MeCl_2$ exposure (Nitschke et al., 1980). Total numbers of benign mammary tumors were increased in all groups of female rats that were exposed to $MeCl_2$. The researchers suggested, upon examination of data from several other studies, that animal housing may have played a confounding role in the increase in the incidence of benign mammary tumors. A few other types of neoplastic lesions were statistically significantly increased or decreased in $MeCl_2$-exposed groups in comparison with the control group; the researchers stated that, based on historical control data for the Sprague-Dawley strain of rats, these values were within the expected range of normal variability.

Except for those of the liver and mammary gland, no gross or histopathologic lesions due to exposure to 500 ppm $MeCl_2$ were observed in female rats treated only for 12 months at the beginning or at the end of the study (Nitschke et al., 1982). The number of rats with 2 lesions was increased in the group treated only for the first 12 months of the study. An increase in the number of rats with multinucleated hepatocytes was increased significantly in the rats in this group that survived to the terminal necropsy. This increase was significant in comparison to controls when the results with these rats were combined with those from moribund rats or rats that died spontaneously during the study, but the observed increase was similar to that in rats exposed to 500 ppm $MeCl_2$ for 24 months. An increase in the percentage of rats with multinucleated hepatocytes was not observed in the group of female rats exposed to 500 ppm $MeCl_2$ only for the second 12 months of the study. There was an apparent increase in the number of rats with benign mammary tumors, including adenomas, fibroadenomas, and fibromas, and in the total number of benign mammary tumors in the group of female rats exposed to 500 ppm $MeCl_2$ only for the first 12 months of the study. This group had a higher percentage of rats with benign mammary tumors than the group exposed to 500 ppm $MeCl_2$ for 24 months; this was believed to be due to the smaller sample size and higher survival rate of the former. In summary, similar lesions were observed in rats exposed to 500 ppm $MeCl_2$ for only the first 12 months of the study and in rats exposed for the whole 24 months. Rats exposed to 500 ppm $MeCl_2$ for only the last 12 months of the study did not develop definite exposure-related lesions by the end of the study. The researchers suggested that these observations were due to differences in the responses of younger and older rats.

The researchers concluded that exposure of rats to 500 ppm $MeCl_2$ resulted in minimal hepatic changes and benign mammary tumors in female rats (Nitschke et al., 1982). Exposure to 200 ppm $MeCl_2$ resulted in an equivocal increase in the percentage of rats with multinucleated hepatocytes. There was no indication of a toxic response following exposure of rats to 50 ppm $MeCl_2$ by inhalation.

## INTRAPERITONEAL STUDY

Doses of 160, 400, and 800 mg/kg $MeCl_2$ in Tricaprylin were injected intraperitoneally 3 times a week, for a total of 17, 17, and 16 injections, respectively, into groups of 20 strain A/St male mice (Theiss et al., 1977). Total doses were 2720, 6800, and 12800 mg/kg, respectively. The mice were killed, the lungs were removed, and surface adenomas counted 24 weeks after the first injection. Of the 20 mice in each group, 18 survived the 160 mg/kg dose, 5 the 400 mg/kg dose, and 12 the 800 mg/kg dose of $MeCl_2$. The number of pulmonary adenomas in the treated mice was not significantly greater than the number in the vehicle-treated controls, although the numbers were elevated at all 3 doses. The response at the 160 mg/kg was almost significant. The researchers suggested that $MeCl_2$ might be carcinogenic in a large-scale test (Table 11).

## PHARMACOKINETICS

$MeCl_2$ was not carcinogenic in 2 oral studies and 2 inhalation studies with rats, and in an inhalation study with hamsters. There was "some evidence of carcinogeniciy" in female rats in 1 inhalation study. $MeCl_2$ was not carcinogenic in 1 oral study with mice. In another oral study, in a report that was not released due to data discrepancies, there was a marginal but significant increase in lung tumors in female mice. In an inhalation study, there was "clear evidence of carcinogenicity" in male and female mice. There was a positive trend in pulmonary adenomas in male mice in an intraperitoneal study.

Extrapolation of these animal data to the human is complex. Relatively recently, physiologically based pharmacokinetic models have been used to facilitate this extrapolation process. These models require relevant base line data on physiological parameters (for example, organ volume, blood flow, etc.) and biochemical constants for metabolism and tissue binding of the test compound. Enzymatic constants also are required so that the role of metabolism of the test chemical can be evaluated with the model. The background for such an approach has been described in several publications (Andersen, 1981; Andersen et al., 1984; Clewell and Andersen, 1985; Ramsey and Andersen, 1984). Recently, Andersen et al. (1986) and Reitz and Andersen (1985) developed a physiologically based pharmacokinetic model for $MeCl_2$

which may prove useful in the risk assessment process. This model was designed to provide a rational basis for the conversion of the "external or exposure dose" of $MeCl_2$ to an appropriate "internal dose" which is more toxicologically relevant. Further, this analysis assists in the problem of extrapolation of the data obtained in the studies on the mouse, the hamster, and the rat to human risk assessment. This analysis demonstrated that the tumor incidence in the two chronic studies of $MeCl_2$ in mice was correlated with various measures of target tissue dose of the test compound. Specifically, tumor incidence correlated with the amount of $MeCl_2$ metabolized by the glutathione S-transferases (GST) and not with $MeCl_2$ metabolized by the mixed function oxidases. A similar approach based on human exposure to $MeCl_2$ suggests that conventional risk analysis greatly overestimates the risk in humans exposed to relatively low concentrations of $MeCl_2$. These data suggest that the high incidence of tumors in the mouse bioassays may not be a reasonable predictor of human toxicity for $MeCl_2$. Furthermore, recent metabolism data conducted both in vivo in mice and rats and in vitro with liver and lung tissue from rats, mice and hamsters and liver tissue from humans also are consistent with this conclusion (ICI, 1986b; 1986f; 1986g). The mouse appears to have significant GST mediated $MeCl_2$ metabolism in the liver with the rate being 12-fold greater than that of rat liver. No such metabolism was found in either hamster or human liver. A low rate of GST metabolism also was present in mouse lung tissue, but not in rat or hamster lung. (Although no data is available, the Expert Panel is aware, that with more sensitive radiochemical technique, measurable concentrations of GST have been detected in mouse, rat, hamster, and human tissues and, that the rank order of enzyme activities is: mouse >> rat > hamster and human (ICI, 1987). It is the GST pathway that is thought to be associated with carcinogenesis. Along with the kinetic data, these observations suggest little risk for man to develop cancer with exposure to $MeCl_2$. Further, the metabolism data suggest that the hamster may be the best model for human $MeCl_2$ carcinogenicity studies.

### IARC REPORT

The 1986 and 1987 pharmacokinetic data contained in this report were not evaluated in the 1986 International Agency for Research on Cancer (IARC) report. IARC evaluated other available data and concluded that "There is 'sufficient evidence' for the carcinogenicity of dichloromethane to experimental animals. There is 'inadequate evidence' for the carcinogencity of dichloromethane to humans." IARC also stated that "In the absence of adequate data on humans, it is reasonable, for practical purposes to regard chemicals or exposures for which there is 'sufficient evidence' of carcinogenicity in animals as if they presented a carcinogenic risk to humans."

## CLINICAL ASSESSMENT OF SAFETY

### EXPERIMENTAL EXPOSURE

Men and women have been exposed experimentally to $MeCl_2$ by inhalation (Fodor and Winneke, 1971; Forster et al., 1974; Gamberale et al., 1975; Hake et al., 1974; Putz et al., 1979; Stewart et al., 1972a; 1972b; 1973; Winneke et al., 1975) (Table 14). Subjects have also immersed their thumbs in liquid $MeCl_2$ under experimental conditions (Stewart and Dodd, 1964) (Table 12).

The effects of a deodorant containing 21.5% $MeCl_2$ and an antiperspirant containing 20.0% $MeCl_2$ were evaluated following 12 weeks of twice daily usage by 47 men and 28 women and 25 men and 24 women, respectively (Meltzer et al., 1977). A dermatologist evaluated skin reactions at 1, 2, 4, 8, and 12 weeks. Very slight transient erythema was observed at random examination periods. The "reactions were reported to be normal, negligible, and not necessarily product-induced."

## OCCUPATIONAL EXPOSURE

Thirty-three accidental industrial exposures to $MeCl_2$ that resulted in death or disablement for 3 or more days were reported to Her Majesty's Factory Inspectorate in Great Britain from 1961 to 1980 (Bakinson and Jones, 1985). Eight humans in confined areas and 5 in non-confined areas became unconscious. Twenty humans remained conscious, 6 were in confined areas and 14 were in non-confined areas. One unconscious human died; death was attributed to acute narcosis resulting in respiratory depression, and there was evidence of hepatic and splenic congestion. Of the survivors, effects on the central nervous system, including headaches, dizziness, confusion, incoordination, and paraesthesia, were reported in 19 humans, effects on the gastrointestinal system, including nausea, in 13 humans, and effects on the respiratory system in 4 humans. Hepatic tenderness was reported in 1 human, but the results of a liver function test was normal. The researchers stated that no substantial evidence for a hepatorenal or cardiac effect was found.

A study was conducted with 46 men who worked in a factory making acetate film and who were exposed to 9:1 $MeCl_2$:methanol (Cherry et al., 1981). The concentration of $MeCl_2$ in the air ranged from 75 to 100 ppm. Twelve men who also worked in the factory, but were not exposed to solvents, served as controls. There was an excess of self-reported neurological symptoms. A follow-up study was conducted with 29 of the exposed men. These men were

TABLE 12

EXPERIMENTAL EXPOSURE

| $MeCl_2$ Concentration | Method | Results and Comments | References |
|---|---|---|---|
| 0 to 500 ppm | 4 human males were exposed to $MeCl_2$ by inhalation 7.5 hr per day for 26 days over a 6-wk period. The effect on pulmonary function was determined. | $MeCl_2$ had no effect on the functional integrity of the pulmonary airways, on pulmonary gas exchange, and on regulation of pulmonary ventilation. | Forster et al., 1974 |
| 250 to 1000 ppm | 14 human males were exposed to 4 consecutive 30 min periods of 250, 500, 750, and 1000 ppm $MeCl_2$, respectively, by inhalation. Heart rates were measured and performance tests performed in the final 20 min of each exposure period. The performance tests included a numerical ability and reaction time test, two simple reaction time tests, and a short-term memory test. Subjective symptoms were recorded following exposure. The men served as their own controls. | Exposure to $MeCl_2$ exerted a subjectively favorable change in the men's experience of condition. With a few exceptions, heart rate was lower, but not significantly, during exposure. The performance test results were not systematically different from the results under control conditions. Following exposure to 1000 ppm $MeCl_2$, there was a greater irregularity in performance but no change in average reaction time. The researchers stated that brief exposure to $MeCl_2$ had no ill effect on the psychomotor and cognitive functions of men. | Gamberale et al., 1975 |
| 250 ppm | 4 human females were exposed to $MeCl_2$ by inhalation for 7.5 hr per day, 2 including one smoker for 3 hr per day, and 3 for 1 hr per day for 5 days. Subjects exposed to $MeCl_2$ for 1 or 3 hr per day exercised mildly on bicycle ergometers for 5 and 10 min, respectively, each day during exposure. Neurological, behavioral, and medical tests were conducted before, during, and after exposure. | Exposure to $MeCl_2$ did not affect subjects' health. There were a greater number of subjective complaints of mild headache and mild nausea during exposure to $MeCl_2$ than during 2 days of non-exposure. One subject vomited during hr 7 of the day 5 7.5 hr exposure. There were no detectable changes in electroencephalograms (EEG) or in visual evoked response (VER) or in the results of an alertness test following $MeCl_2$ exposure. No deleterious effects were observed in other neurological, behavioral, and medical tests. | Nake et al., 1974 |
| 200 ppm | 6 human male and 6 female non-smokers were exposed to $MeCl_2$ by inhalation for 4 hr 3 times at 7 day intervals. Subjective symptoms were recorded and performance in a dual-task activity, an eye-hand coordination task performed concurrently with peripheral brightness monitoring, and in an auditory vigilance task was measured. | Following MeCl- exposure, the performance of subjects of difficult and demanding tasks deteriorated. There was an impairment in performance of all the tasks; a decrease in the speed and precision of psychomotor performance was observed. | Putz et al., 1979 |
| 213 ppm | 1 human male non-smoker was exposed to $MeCl_2$ by inhalation for 1 hr. Subjective symptoms were recorded and clinical hematological and chemical studies were performed. | No untoward subjective symptoms or objective signs of illness were noted during exposure or during the 24 hr period following exposure. Hematocrit remained stable and all results of clinical hematological and chemical studies were normal. | Stewart et al., 1972a; 1972b |
| 986 ppm | 3 human male non-smokers were exposed to $MeCl_2$ by inhalation for 2 hr. Subjective symptoms were recorded, VER measured, and clinical chemical and hematological studies were performed. | No eye, nose, or throat irritation was reported. After 1 hr, two subjects reported mild light-headedness. One subject had a "thick tongue" and difficulty in enunciating. Light-headedness cleared within 5 min after exposure was terminated. VER was altered in all subjects and shifted towards control responses within 1 hr after exposure. Hematocrit values and all clinical chemical and hematological values were normal. There was no increase in urinary urobilinogen formation. | Stewart et al., 1972a; 1972b |

TABLE 12 - Continued)
EXPERIMENTAL EXPOSURE

| $MeCl_2$ Concentration | Method | Results and Comments | References |
|---|---|---|---|
| 514 to 868 ppm | 3 human male non-smokers were exposed to 514 ppm $MeCl_2$ for 1 hr and 868 ppm $MeCl_2$ for a second hr by inhalation. Subjective symptoms were recorded and VER was determined. Hematological, clinical chemistry, and 24 hr urinary urobilinogen values were measured. | One subject reported being light-headed within 15 min of exposure to 868 ppm. This subsided 5 min following exposure. No other subjective symptoms were recorded. VER was altered during exposure and shifted toward control responses following exposure. Hematological values, clinical chemistry values, and urinary urobilinogen values were normal during the 24 hr period following exposure. | Stewart et al., 1972a; 1972b |
| 515 ppm | 8 human male non-smokers were exposed to $MeCl_2$ by inhalation for 1 hr. Subjective symptoms were recorded and hematological and clinical chemistry studies were performed. | No untoward subjective symptoms or objective signs of illness were noted. There was no evidence of an increase in red blood cell destruction. The researchers stated that a symptom of central nervous system depression, alteration of VER, was observed in some subjects exposed to 500 to 1000 ppm $MeCl_2$ (see above table entries with same reference). | Stewart et al., 1972a; 1972b |
| 0 to 500 ppm | 4 human males were exposed to $MeCl_2$ by inhalation for 7.5 hr per day, 3 for 3 hr per day, and 3 for 1 hr per day, 2 to 5 days per week for 5 weeks. One subject in each group was a smoker. Medical examination, urinalysis, clinical chemistries, and electrocardiograms (EKG) were performed daily or weekly. Electroencephalograms (EEG) were performed and VER was measured. A neurological test, the equilibrium test, and behavioral tests, an alertness test, 10 and 30 sec estimation tests, a marquette estimation test, a coordination test, an arithemetic test, and an inspection test were also performed. | No deleterious health or behavioral effects were seen following inhalation of $MeCl_2$. | Stewart et al., 1973 |
| 300 and 800 ppm | 12 human females were exposed to $MeCl_2$ by inhalation for 3 hr. An auditory vigilance task and a sensory task of critical flicker frequency (CFF) for the measurement of cortical alertness were performed. | Auditory vigilance and CFF were critically impaired following exposure to $MeCl_2$. | Fodor and Winneke, 1971;<br>Winneke et al., 1975 |
| 800 ppm | 18 human females were exposed to $MeCl_2$ by inhalation for 4 hr. An auditory vigilance task and several psychomotor tests to study the speed and accuracy of of visual-motor performance were conducted. | Auditory vigilance was significantly impaired. There was a generalized impairment of psychomotor performance; motor speed of gross hand and arm movements was reduced, reaction times for simple and complex responses were increased, coordination and precision of complex movement patterns and the ability to react rapidly to changing stimulus configurations were impaired, and the steadiness and control precision of static and dynamic positioning movements were disturbed. | Winneke et al., 1975 |
| Liquid $MeCl_2$ | 4 subject immersed their thumbs in liquid $MeCl_2$ for 30 min. | All subjects experienced an "intense burning sensation on the dorsum of their thumbs" within 2 min. Within 10 min all felt a "numb, cold feeling as if the thumb had been subjected to a nerve block. The slightest movement ... triggered waves of searing pain. Following removal ... thumbs felt 'numb and cold as if asleep'." Mild erythema and a slight degree of white scale were observed on the thumbs after removal from the $MeCl_2$. The erythema and parathesia subsided within 1 hr. | Stewart and Dodd, 1964 |

age-matched within 3 years to 29 control men from another factory who were not exposed to solvents. Upon clinical examination, no difference of any significance was found between the 2 groups of men. $MeCl_2$ exposure did not seem to be related to cardiac abnormalities. Motor conduction velocities were measured in the ulnar and median nerves, an EEG was taken, and a psychological test battery to detect minimal brain damage was administered. No evidence of long-term damage that could be attributed to $MeCl_2$ was observed.

A study was conducted with 56 men who worked in a factory making acetate film and who were exposed to 9:1 $MeCl_2$:methanol (Cherry et al., 1983). The concentration of $MeCl_2$ in the air ranged from 28 to 173 ppm. Thirty-six men, unexposed to solvents, from this and another factory served as controls. Tests were conducted at the beginning and at the end of each shift; these tests included visual analogue scales to reflect mood, the digit symbol substitution test, and a simple reaction time test to reflect performance. In addition, blood samples were assayed for solvent concentration. Exposed men deteriorated more over the shift than the controls did in terms of sleepiness, physical tiredness, and mental tiredness; differences were significant statistically only for the morning shift. Exposed men deteriorated more, but not significantly, over the night shift than the controls did in terms of general good health. On the whole, greater deterioration in mood over a shift was associated with higher blood solvent concentrations at the end of the shift. There was no difference in deterioration over the shift in the performance of exposed and control men on the performance tests. However, performance deterioration on the digit symbol substitution test for exposed men was related to the end-of-shift blood solvent concentrations.

The accidental occupational exposure of 4 men to $MeCl_2$ for about 1 to 3 hours has been reported; 1 man died, but the other 3 recovered after varying periods of unconsciousness (Moskowitz and Shapiro, 1952). Irritation of the eyes and upper respiratory tract, irritation of the bronchi and lungs, and possible adverse effects on the hemopoietic system were observed.

## EPIDEMIOLOGY

Epidemiological studies have been conducted for $MeCl_2$. In one study, $MeCl_2$ had been used as the primary solvent in the operations of a department of a chemical company continuously for more than 30 years (Friedlander et al., 1978; Hearne et al., 1987). The time-weighted average (TWA) $MeCl_2$ concentration ranged from 30 to 120 ppm and the concentration was sometimes as high as about 150 ppm. Two different approaches to mortality data were used; the proportionate mortality ratio (PMR) approach was used to allow for the study of all 1956 to 1976 death certificates attributed to former employees of the $MeCl_2$ work area, and a noncurrent or historical prospective review of the 1964 $MeCl_2$ area cohort was also conducted. The complete 1964 $MeCl_2$ area cohort was reviewed with no criteria of latency, and employees who first worked in the $MeCl_2$ area before 1964 were reviewed with a 20-year latency criterion. These employee cohorts were also followed through 1976, for a maximum of 13 years. The PMR analysis of 334 deaths indicated no significant excess causes of deaths either by major diagnostic groups or by malignancy subgroupings. In the cohort mortality study, 751 male employees were compared to industrial controls; there was no significant increase in deaths in total, major group, or diagnostic subgroup categories. Both total malignancies and circulatory disease deaths were less than expected. In comparison with New York state, exclusive of New York City, controls, the 20-year cohort had significantly lower mortality from all causes, including total malignant neoplasms, respiratory cancer, and total circulatory and ischemic heart disease. Results of life table analysis indicated that the $MeCl_2$-exposed employees had a greater probability of surviving 13 years than either the New York state control or United States national controls. Over all the years of follow-up, for all age groups, the probability of surviving for the $MeCl_2$-exposed employees was not significantly different from that for the industrial controls. An additional 4 year follow-up to 1980 was conducted with the 1964 cohort of employees who had been exposed to $MeCl_2$ (Hearne and Friedlander, 1981; Hearne et al., 1987). The results of the follow-up supported the conclusions of the original study; the mortality of the $MeCl_2$-exposed employees was consistent with the industrial controls and was less than the New York state general population. Total numbers of malignancies and circulatory diseases, including ischemic heart disease, were lower than expected, in comparison with New York state controls. There was a marginally significant decrease in respiratory malignancies in long-term exposed employees when compared with New York state controls. An additional follow-up describes the results of chronic $MeCl_2$ inhalation on these chemical company employees through 1984 (Friedlander et al., 1986; Hearne et al., 1987). The 1013 male employees evaluated had a mean $MeCl_2$ exposure of 22 years and a latency of 30 years. There were no significant excess deaths, and there was no evidence of a dose-response relationship for neoplasms of the lung and liver or ischemic heart disease. Predictions from bioassays with animals were compared with epidemiologic findings in humans. The predicted number of respiratory and hepatic malignancy deaths in humans was significantly more than the number actually observed. The study had sufficient statistical power to detect relative risks for pulmonary cancer and cardiovascular disease, but did not have sufficient statistical power to address breast and hepatic cancer deaths (Friedlander et al., 1985; Hearne et al., 1987).

In another epidemiological study, male and female employees of a plant that produced cellulose diacetate and cellulose triacetate fibers, and who were exposed to $MeCl_2$, methanol, and acetone were studied (Ott et al, 1983b; 1983c; 1983d; 1983e). These employees were compared with employees at a reference plant that manufactured cellulose diacetate, and who were not exposed to $MeCl_2$. The research project included a hygiene survey of both plants, a mortality study of both employee populations using a retrospective cohort design including follow-up of employees who had left the plants, a health evaluation of both employee populations, and an analysis of continuous ambulatory EKGs for men over 34 years of age. An industrial survey was performed during 1977 and 1978; in the plant in which employees were exposed to $MeCl_2$, the ratio of methanol to $MeCl_2$ was 1 to 10. The exposed population was divided into 3 exposure categories: low $MeCl_2$ or a TWA of 140 ppm and high acetone or a TWA of 1080 ppm, moderate $MeCl_2$ or a TWA of 280 ppm and low acetone or a TWA of 110 ppm, and high $MeCl_2$ or a TWA of 475 ppm and low acetone or a TWA of ~~1~~10 ppm. The reference population was also divided into 3 categories: low acetone or a TWA of 380 ppm, moderate acetone or a TWA of 770 ppm, and high acetone or a TWA of 1070 ppm. The mortality study included 1271 $MeCl_2$-exposed employees and 948 reference employees who had worked at least 3 months at the plants between January 1, 1954 and June 1977. In comparison with the mortality of the general United States population, there was no significant increase in overall mortality or in seaths due to malginant neoplasms or to ischemic heart disease. Incidences of ischemic heart disease were further analyzed by employment status, exposure duration, and follow-up interval; there was no exposure-related effect. No mortality effects that could be attributed to $MeCl_2$ were observed. Health evaluation studies were voluntary, and 266 $MeCl_2$-exposed employees and 251 reference employees participated. An increase was observed in red cell counts, hemoglobin, and hematocrit among females but not human males exposed to about 475 ppm $MeCl_2$; this was suggestive of a compensatory hematopoietic effect. No increase was observed in mean corpuscular volume and mean corpuscular hemoglobin. There was a dose-related increase in serum bilirubin in both male and female employees exposed to $MeCl_2$, but there was no corresponding pattern of changes in other serum and blood constituents consistent with either hepatic injury or hemolysis. The ᴇKGs of 24 $MeCl_2$-exposed and 26 non-exposed 37 to 63 year old white males were monitored for 24 hours. The TWA for the exposed employees ranged from 60 to 475 ppm $MeCl_2$. There was no increase in ventricular or supraventricular ectopic activity or episodic ST-segment depression associated with exposure to $MeCl_2$.

A case-control study was conducted with 38 women who had had spontaneous abortions during employment in Finnish pharmaceutical factories during 1973 or 1975 to 1980 (Taskinen et al., 1986). Three age-matched employees of pharmaceutical factories who had given birth to children were controls for each case. Based on 11 exposed cases and 17 exposed controls, the increase in the odds ratio for $MeCl_2$ exposure was of borderline significance. The odds ratio for $MeCl_2$ increased with frequency of use; the odds ratio was 2.8 for exposure once a week or more and 2.0 for exposure less than once a week.

An elevated incidence of pulmonary cancer has been observed in female cosmetologists. A case-control study was conducted in Los Angeles County to investigate the effects of occupational and environmental factors on lung cancer risk (Osorio et al., 1986). There were no significant differences between case and control cosmetologists in various demographic factors, specific beauty shop tasks, and specific beauty product use, including hair spray use. Data uncertainties prevented analyses based on duration of specific beauty shop tasks and specific beauty product use. There was an association between lung cancer and smoking and jobs other than employment as beauticians. Lack of data about other workplaces prevented further interpretation, but the researchers stated that other employment was unlikely to explain the greater risk for lung cancer in cosmetologists, and that the excess pulmonary cancers observed in female cosmetologists were probably attributable to excess smoking. Several other studies have investigated the relationship between employment as a beautician and incidence of cancer, but none of these studies examined smoking status (Garfinkel et al., 1977; Kono et al., 1983; Menck et al., 1977; Teta et al., 1984).

## SUMMARY

$MeCl_2$ is a disubstituted halogenated methane. It is a colorless, volatile liquid. $MeCl_2$ is usually manufactured by the chlorination of methane or methyl chloride followed by distillation.

$MeCl_2$ has industrial, food, medical, and home uses, and it is ubiquitous in the environment. $MeCl_2$ has been used primarily by the cosmetic industry as a component of the aerosol propellant system in hair spray formulations. It has also been used in manicuring preparations, personal cleanliness products, and novelty temporary hair colorings that are applied as sprays. In 1981, cosmetic manufacturers and formulators reported to the Food and Drug Administration that $MeCl_2$ was used in 47 hairsprays at concentrations ranging from 1 to 50% and was used in 1 manicuring preparation in a concentration of 0.1 to 1%. In 1985, there were 71 reported uses of $MeCl_2$. Sixty-nine hairsprays contained 1 to 50% $Mecl_2$. One nail polish and enamel remover and one personal cleanliness product contained unreported concentrations of $MeCl_2$. In 1986, $MeCl_2$ was not reported as an ingredient in any cosmetic product.

Several government agencies, including the Food and Drug Administration, are reviewing the risks to humans of exposure to $MeCl_2$. The Food and Drug Administration has proposed to "ban the use of Methylene Chloride as an ingredient of cosmetic products..." but, based on the _de minimis_ doctrine, to "permit the continued use of Methylene Chloride to decaffeinate coffee..."

$MeCl_2$ is readily absorbed through the lungs and through the skin of humans. Administration of radioactive $MeCl_2$ to rats and mice resulted in widespread dissemination of radioactivity in tissues. Data from tissue distribution studies with mice and rats indicated greater accumulation of radioactivity from radioactive $MeCl_2$ in the liver and kidneys and more rapid elimination of radioactivity from body fat and brain in comparison with other tissues.

Following inhalation of $MeCl_2$ by humans, $MeCl_2$ was detected in blood and adipose tissue. Additionally, $MeCl_2$ has been detected in human placental core blood samples.

Carbon monoxide (CO) was detected in the breath, and carboxyhemoglobin (COHb) was detected in the blood of humans after exposure to $MeCl_2$ by inhalation. Metabolic conversion of $MeCl_2$ to CO, COHb, and carbon dioxide ($CO_2$) has been studied in several species.

The metabolism of $MeCl_2$ is enzyme-catalyzed and, therefore, has capacity-limited phenomena at high concentrations. First order kinetics are observed at low $MeCl_2$ concentrations and zero-order kinetics are observed at high concentrations. Because of the saturable character of $MeCl_2$ metabolism, the difference between administered dose and effective dose becomes greater with increasing exposure doses.

The overall time course for $MeCl_2$ metabolism is complex due to contributions from at least 2 pathways with varying kinetic parameters. Pathway 1, a high affinity, low capacity pathway localized in the hepatic microsomal fraction, is mediated by a cytochrome P-450-dependent monooxygenase system and produces CO. Pathway 2, a low affinity, high capacity pathway found in the hepatic cytosolic fraction, is mediated by glutathione transferase and produces formaldehyde, formic acid, inorganic chloride, and $CO_2$. The $V_{max}$ for $MeCl_2$ metabolism is a composite $V_{max}$ for the 2 pathways. The contribution of the 2 pathways to $MeCl_2$ metabolism depends on the species and organ studied.

Covalent binding of radioactivity from radioactive $MeCl_2$ has been observed _in vivo_ in the livers of mice and _in vitro_ in hepatic lipid and protein molecules of rats. No alkylation of DNA or RNA was observed in these studies or in other studies in which DNA was isolated from the liver, lungs, or salivary glands of rats, mice, and hamsters exposed to $MeCl_2$ by inhalation. The metabolic conversion of $MeCl_2$ to 1-carbon fragments may provide appreciable potential for the incorporation of those fragments into a variety of endogenous substrates involved in normal intermediary and synthetic metabolism.

Following exposure to $MeCl_2$, $MeCl_2$ was eliminated in the breath, urine, or feces of rats, mice, dogs, and humans.

Several factors influence $MeCl_2$ uptake, distribution, metabolism, and excretion in humans; these include smoking, level of physical exercise, and chronic pulmonary and cardiovascualr problems.

The single-dose LD50 for $MeCl_2$ administered orally to adult rats ranged from 1.06 to 2.3 ml/kg. $MeCl_2$ was administered orally to mice in short-term tests and to rats and mice in subchronic tests and rats in chronic tests, and was administered dermally to rats in acute tests; few effects due to $MeCl_2$ were observed. $MeCl_2$ was irritating to the skin of rabbits and was moderately irritating to the eyes of rabbits. $MeCl_2$ has been studied in acute, subchronic, and chronic inhalation studies using rats, mice, rabbits, gerbils, guinea pigs, hamsters, cats, dogs, and monkeys. Results of these studies varied with $MeCl_2$ concentration and duration of exposure. In some studies, no adverse effects were observed. In other studies, anaesthetic effects were noted and, in some cases, animals died after exposure to high doses of $MeCl_2$. No signs of toxicity were observed when monkeys were exposed to a deodorant spray containing $MeCl_2$ in a subchronic test. Teratogenicity studies have been conducted with $MeCl_2$ in the drinking water and in the feed of rats; $MeCl_2$ was not teratogenic in these studies. The potential teratogenicity of $MeCl_2$ has been studied in rats, mice, rabbits, and dogs; generally, $MeCl_2$ was not teratogenic in these studies.

Both positive and negative results have been obtained with $MeCl_2$ in the Salmonella/mammalian-microsome mutagenicity test. Results appear to vary primarily with the protocol followed. $MeCl_2$ was generally negative in the standard plate incorporation test and was positive when plates without $MeCl_2$ incorporated in the media were incubated in air-tight chambers, and $MeCl_2$ was introduced into the chambers. $MeCl_2$ has been tested in a variety of other short-term tests predictive of mutagenicity and carcinogenicity, and both positive and negative results have been obtained.

The National Coffee Association has sponsored carcinogenicity studies in which $MeCl_2$ was administered in the drinking water of Fischer 344 rats and $B6C3F_1$ mice at doses of up to 250 mg/kg/day for 24 months. A slight increase in proliferative hepatocellular lesions, adenoma, and carcinoma was observed in treated male mcie, but this response was within the range of $B6C3F_1$ mouse historical control data for the laboratory and that reported in the scientific literature. The researchers stated, that under the conditions of these studies, $MeCl_2$ was not carcinogenic for rats or mice.

The National Toxicology Program (NTP) conducted a 2 year carcinogenicity study in which $MeCl_2$ in corn oil was administered by gavage to rats and mice. The draft report of this study will not be issued as a final report due to discrepancies in experimental data that compromise a clear interpretation.

Coffee, from which caffeine had been removed by extraction with $MeCl_2$, was given at a dose of 6% to rats in the feed for 2 years. The coffee was not reported to be carcinogenic for the rats.

F344/N rats were exposed to up to 4000 ppm $MeCl_2$ by inhalation 6 hr a day for 2 years in a study conducted by NTP. There were significant positive trends in the incidences of mammary gland fibroadenomas in treated male and female rats, and the incidences were significantly increased in high dose rats. There were also significant trends in the incidences of subcutaneous fibromas and combined fibromas and sarcomas in treated male rats, but the incidences were not significantly increased. A significant positive trend was observed in the incidences of hepatic neoplastic nodules and combined neoplastic nodules and hepatocellular carcinomas in treated female rats, but the incidences were not significantly increased. Mesotheliomas of the tunica vaginalis or multiple organs occurred with a significant positive trend in treated male rats, and the incidences were significantly increased in mid-dose and high dose rats. A significant positive trend was observed in the occurrence of mononuclear leukemia in treated male and female rats, and the incidences were significantly increased in mid-dose and high dose rats. The incidences of adrenal gland pheochromocytomas and interstitial cell tumors of the testes in male rats, and combined pituitary gland adenomas and carcinomas in treated male and female rats were marginally significantly increased. Squamous metaplasia of the nasal cavity was observed in an increased incidence in high dose treated female rats. Splenic fibrosis was observed in increased incidences in treated male and female rats, and hyperplasia of the parathyroid was observed in increased incidence in treated male rats. The NTP concluded that there was "some evidence of carcinogenicity" for $MeCl_2$ in female rats, as indicated by increased incidences of mammary gland neoplasms.

$B6C3F_1$ mice were exposed to up to 4000 ppm $MeCl_2$ by inhalation 6 hr a day for 2 years in a study conducted by NTP. Significant positive trends were observed in the occurrence of alveolar/bronchiolar adenomas and alveolar/bronciolar carcinomas in treated male and female mice, and the incidences were significantly increased. The number of treated mice with multiple lung tumors increased in a dose-related manner. The incidences of hepatocellular adenomas and hepatocellular carcinomas occurred with signficant positive trends in treated male and female mice, and some of these incidences were significantly increased. The incidence of multiple hepatocellular tumors in treated mice was dose-related. There were significant positive trends in the incidences of hemangiosarcomas and combined hemangiomas and hemangiosarcomas in treated male mice, and the incidences were significantly increased. The NTP concluded that there was "significant evidence of carcinogenicity" of $MeCl_2$ for male and female mice, as indicated by increased evidence of aveolar/bronchiolar and hepatocellular neoplasms.

Sprague-Dawley rats were exposed to up to 3500 ppm $MeCl_2$ by inhalation 6 hr a day for 2 years. There was an increased incidence of hepatocellular necrosis in mid-dose and high dose male rats. An increased number of benign mammary tumors per tumor-bearing treated female rat was observed. The total number of female rats with benign mammary tumors was not significantly increased in any group, although the total number did increase in an exposure-related manner. Benign mammary tumors, dose-dependent in number, were also observed in male rats but not to same extent as in female rats. There was no indication of a progression from benign to malignant mammary tumors, and Sprague-Dawley rats have a predisposition towards benign mammary tumors. The cumulative number of neoplasms, either benign or malignant, was not different in control or exposed female rats. With exposure to $MeCl_2$, an increased number of sarcomas in and around the salivary glands of male rats was observed, but the relevance of this result is uncertain. The researchers did not conclude that $MeCl_2$ was carcinogenic to rats.

Golden Syrian hamsters were exposed to up to 3500 ppm $MeCl_2$ by inhalation 6 hr a day for 2 years. There was no $MeCl_2$-exposure related difference observed in male hamsters in the total number of animals with neoplasms, the total number with benign neoplasms, and the total number with malignant neoplasms. There was a significant increase in benign neoplasms in high dose female hamsters, but this was considered to be secondary to the increased survival of this group. The researchers did not conclude that $MeCl_2$ was carcinogenic to hamsters.

Sprague-Dawley rats were exposed to up to 500 ppm $MeCl_2$ by inhalation 6 hr a day for up to 2 years. The percentage of treated female rats with benign mammary tumors, including adenomas, fibroadenomas, and fibromas, increased in a dose-dependent manner with $MeCl_2$ exposure. Total numbers of benign mammary tumors were increased in all exposed female rats. The researchers concluded that the increased benign mammary tumors in female rats were the result of exposure to $MeCl_2$. The researchers suggested, upon examination of data from several other studies, that the animal housing may have played a confounding role in the increase in the incidence of benign mammary tumors. A few other types of neoplastic lesions were significantly statistically increased in exposed rats, but based on historical control data for Sprague-Dawley rats, these incidences were within the expected range of normal variability.

Doses of up to 800 mg/kg $MeCl_2$ were injected intraperitoneally 3 times a week for up to 6 weeks into A/St male mice. There was a positive trend in the incidence of pulmonary adenomas in treated mice. The researchers suggested that $MeCl_2$ might be carcinogenic in a large-scale test.

Extrapolation of animal data from carcinogenesis studies to the human is complex. Relatively recently, physiologically based pharmacokinetic models have been used to facilitate this extrapolation process. Specifically, tumor incidence has been correlated with the amount of $MeCl_2$ metabolized by the glutatione S-transferases (GST) and not with the mixed function oxidases. The mouse, the only species in which $MeCl_2$ was carcinogenic, has significant GST mediated $MeCl_2$ metabolism in the liver with the rate being 12-fold greater than that of rat liver. No such metabolism was found in either hamster or human liver. A low rate of GST metabolism also was present in mouse lung tissue, but not in rat or hamster lung. Along with kinetic data, these observations suggest little risk for humans to develop cancer with exposure to $MeCl_2$.

Men and women have been exposed experimentally to $MeCl_2$ by inhalation. In some studies, no adverse effects were observed. In other studies, subjects reported headaches and "light-headedness" and nausea, and task performance deteriorated. Subjects have also immersed their thumbs in liquid $MeCl_2$ under experimental conditions; mild erythema and a slight degree of white scale were observed. A deodorant and an antiperspirant containing $MeCl_2$ caused very slight transient erythema during normal usage.

Accidental industrial exposures to $MeCl_2$ have resulted in death or disablement in some cases. No significant effects that could be attributed to $MeCl_2$ were observed in factory-workers who were exposed to $MeCl_2$ in one study. In another study, $MeCl_2$ did have a slight effect on the performance of factory-workers who were exposed to $MeCl_2$.

Two epidemiological studies have been conducted to determine the toxicity of $MeCl_2$ for humans. No significant excess deaths were observed in either study, and there were no significant increases in malignant neoplasms or ischemic heart disease.

in a case-control study of spontaneous abortions in women employed in Finnish pharmaceutical factories, the odds ratio for $MeCl_2$ exposure was of borderline significance.

Excess pulmonary cancers in female cosmetologists have been attrributed to smoking and not to specific beauty shop tasks or specific beauty products use.

## DISCUSSION

$MeCl_2$ is a volatile compound that, if applied as an aerosol, would not remain on the skin for an extended period of time. However, certain cosmetic products that contain $MeCl_2$ are designed to remain on the skin and, thus may expose the skin to $MeCl_2$ for longer time periods. It has been estimated that the use of hair sprays containing $MeCl_2$ could expose the user to $MeCl_2$ concentrations ranging from 1 to 154 μg/liter of air.

$MeCl_2$ was irritating to the skin of animals; an antiperspirant and a deodorant containing $MeCl_2$ were mildly irritating to the skin of humans. Limited data obtained from animal and human studies indicated that $MeCl_2$ did not induce sensitization. No data were available on whether $MeCl_2$, when applied in a medium designed to remain on the skin is, or is not, a sensitizer. $MeCl_2$ does not absorb UVA or UVB light; therefore, it is unlikely to be a phototoxic agent.

In seven different laboratory studies with sufficient animals to permit meaningful statistical analysis of the data, only the results from a chronic mouse study - indicated that $MeCl_2$ is a carcinogen. Results of pharmacokinetic and metabolism studies established that the metabolism of $MeCl_2$ in the mouse differs quantitatively from other species studied, and this difference in metabolism could account for the positive tumorogenic response in the mouse. Neither the metabolic nor the pharmacokinetic studies identified the actual carcinogenic process to allow rational extrapolation across species. To conclude that the one positive carcinogenicity study is of greater significance in safety evaluation than the six negative carcinogenicity studies, it would be necessary to exclude the results of the pharmacokinetic, metabolism and epidemiological studies that support the conclusion that $MeCl_2$ is not a carcinogen for humans and other animal species.

Considering all the data, and, in particular, the pharmacokinetic and metabolism data, the Panel concludes that data are insufficient to establish $MeCl_2$ as a human carcinogen. Further, the Panel concludes that the positive carcinogenic response obtained in the mouse study cannot be extrapolated to humans. The evidence is that $MeCl_2$ is a carcinogen for mice, but is not carcinogenic for rats, hamsters or humans.

Due to the lack of human skin irritation and sensitization data on cosmetic products containing $MeCl_2$, the Expert Panel is restricting its conclusion to aerosol products in which the duration of exposure (skin contact) is limited by the rapid evaporation of $MeCl_2$ from the skin.

## CONCLUSION

On the basis of the data included in this report, the CIR Expert Panel concludes that $MeCl_2$ is safe for use in cosmetic products designed for brief discontinuous use.

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September 8, 1988

House Small Business Subcommittee on Regulation and Business Opportunities
Subcommittee at Room B-363
Rayburn House Office Building
Washington, DC 20515

Dear Subcommittee,

We are a manufacturer of hair care products. We sell under the name of Paul Mitchell Systems. We test our products on hair sytlists and not on animals. Our research is thorough enough that we our confident and very successful at testing on those that buy, use and sell our products, professional hairdressers.

My recommendation is that cosmetic companies stop testing on animals (which hurts the poor little critters) and have enough confidence in what they are making to test it on themselves and human beings.

Please submit this information at your hearing on September 15, 1988.

Best Regards,

John Paul Jones
Chairman of the Board
JOHN PAUL MITCHELL SYSTEMS

JPJ/jlg

BY THE COMPTROLLER GENERAL

# Report To The Congress

OF THE UNITED STATES

# Lack Of Authority Hampers Attempts To Increase Cosmetic Safety

The Congress should authorize the Food and Drug Administration to require cosmetic manufacturers to prove the safety of their products. Because the agency does not have enough authority to effectively regulate cosmetics, products are being marketed which may pose a hazard to consumers. About 125 ingredients available for use in cosmetics are suspected of causing cancer, and about 25 are suspected of causing birth defects. Although many of the reported adverse effects have not been verified, 30 of the ingredients are known to cause cancer in humans or animals or contain impurities known to cause cancer. The ability of these ingredients to cause toxic effects through cosmetic use has not been determined.

Manufacturers do not have to determine the safety of their products before selling them or tell the Food and Drug Administration what products they are selling and what ingredients are used in them. Many manufacturers have not voluntarily given such information to the agency. As a result, a hazardous cosmetic can be marketed until the Food and Drug Administration obtains information to prove that the product may be injurious to users.

UNITED STATES GENERAL ACCOUNTING OFFICE

HRD-78-139
AUGUST 8, 1978

Access to manufacturers' records

Although the FD&C Act authorizes FDA inspection of cosmetic-manufacturing plants, it does not require manufacturers to permit FDA inspectors to examine their consumer complaint files, safety data, formulation data, shipping records, or other manufacturing records. As a result, manufacturers frequently refuse FDA access to such records. In some cases, FDA inspectors were even refused access to the plants. The following table summarizes the types and numbers of refusals that occurred between fiscal years 1968 and 1976.

| Type of refusal | Number of refusals |
|---|---|
| Access to qualitative or quantitative formulas | 464 |
| Access to sales or shipping records | 75 |
| Access to complaint files | 61 |
| Permit photographing of plant | 33 |
| Access to quality control records | 32 |
| Access to plant except by appointment or other condition | 19 |
| Access to plant | 5 |
| Permit observation of manufacturing procedures | 4 |
| Permit collection of official samples | 4 |

In several cases, FDA inspectors were denied access to complaint files, product formulation, and/or safety data when they were conducting a followup to a consumer complaint.

Civil penalties

The FD&C Act provides for criminal penalties for violations of its cosmetics provisions. However, it may be difficult for FDA to assess criminal penalties for many such violations. FDA has established informal criteria to be used in determining whether to prosecute a manufacturer for violations of the FD&C Act. Among the conditions to be met before prosecution is considered are:

--Prior warning must be given to the firm.

--An individual officer(s) must be identified as responsible for the violation.

UFCW

September 15, 1988

VIA MESSENGER

The Honorable Ron Wyden, Chairman
Subcommittee on Regulation & Business Opportunities
Committee on Small Business
The United States House of Representatives
B-363 Rayburn House Office Building
Washington, D.C. 20515

Dear Representative Wyden:

On behalf of the 40,000 professional hair care workers represented by the United Food and Commercial Workers International Union, AFL-CIO, CLC, we applaud your efforts to examine the safety of the $17-billion cosmetics industry.

As the UFCW testified earlier this summer, the cosmetic products used daily by millions of Americans are mixtures of chemicals, many of which have been linked to serious health problems which include asthma, skin diseases, and neurological damage. Additionally, other long-term effects of these chemicals, in terms of cancer, reproductive disorders, and other debilitating illnesses, need scrutiny.

Most consumers would be shocked to learn that there is no government regulation or testing to assure the safety of cosmetics before they appear on store shelves or are used by hair care professionals. The government has no authority to require cosmetic manufacturers to test their products for safety or effectiveness before they are used in salons or elsewhere. In addition, the Food and Drug Administration has no authority to require that cosmetic manufacturers provide any information to the FDA. The FDA cannot require a cosmetic manufacturer to supply such basic items as ingredient lists, consumer complaints, or test data -- making it almost impossible for the government to determine what chemicals are in cosmetic products, what cosmetics are causing health problems for consumers or workers, or whether the products actually do what the label states. The cosmetic manufacturer is not even required to inform the FDA that a product or even the manufacturer exists.

**William H. Wynn**
International
President

**Jerry Menapace**
International
Secretary-Treasurer

**United Food & Commercial Workers**
**International Union, AFL-CIO & CLC**
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The UFCW hopes your Committee will take steps to close the regulatory loophole that allows this dangerous situation to exist. The UFCW urges prompt consideration of the following steps: (1) New legislation is needed to require, at a minimum, that all cosmetic products, whether sold to consumers or for use in hair salons, must bear ingredient labels; (2) Congress should give the FDA authority to receive all test data, consumer complaints, and ingredient lists from the manufacturers; (3) Congress should give the FDA authority to require registration of cosmetic manufacturers and prouducts; (4) Congress should direct the FDA to establish guidelines for manufacturers to follow in establishing product safety; and (5) Congress should direct the FDA to ban the use of methylene chloride, a potential carcinogen, in hair sprays.

American consumers should be secure in the knowledge that products they purchase off a store shelf or use in a salon have been proven safe before they are put in the marketplace or on their bodies. The measures we have proposed would begin to protect the millions of consumers and workers who use cosmetic products.

Sincerely,

William H. Wynn

International President